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THE HEALTH DEPARTMENT AND THE FOOD OF THE PEOPLE

Chairman's Address

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It is difficult indeed adequately to express how deeply I appreciate the honor of presiding over this section. For many years, bearing various names and under the chairmanship of a long list of distinguished physicians, the annual meetings of this group have afforded a valuable opportunity for those engaged in the administration of official health agencies and those engaged in the practice of preventive medicine to meet together for a discussion of the problems which confront them both.

During the period of my connection with this section, the fields of preventive medicine and public health have moved forward so rapidly that only those of us whose service covers a period of more than one or two decades can recognize how far we have come. Every field of human knowledge, with the possible exception of mathematics, has made more scientific and technologic progress in the last few decades than during the whole of previous history, and public health and preventive medicine have contributed more than their full share in this development. This new knowledge has resulted in profound alterations in the way of life of the human being, and the contribution of preventive medicine to these changes has been most important of all.

It is my purpose at this time, however, to discuss developments in only one small sector of the whole field of public health, that of human nutrition. In that field I shall try to review the changes which have already occurred and to look forward to the problems with which the future is pregnant, so far as they can now be foreseen.

The changes in human food habits during the last three decades have been so rapid, so profound and so powerful in their actual and potential effect on the well-being of the race that they should be far better understood than is now the case. Some of us here can, for example, remember when the food supply of the nation was in large part produced within a few miles of the place of its consumption. Some have, in fact, loaded a sack of corn on the back of a horse or mule and ridden with it to the grist mill and then watched the grain poured into the hopper and in a moment seen the meal running smoothly back into the sack from which the corn had just been poured. I can remember when the fruits and vegetables on sale even in the larger cities were almost all produced on nearby farms. They were brought to the markets of the city and there sold to the consumer by the farmers who had themselves grown and harvested them. Tropical fruits were a great luxury, available, except to the very rich, only on very special occasions.

The supply of milk was from varied sources and was wholly unregulated. Many families in the cities kept one or two cows for their own supply and sold the surplus to their neighbors over the back fence. These one-cow dealers, as they were called, were a problem of serious moment in the early campaigns of milk sanitation. For the rest, the public supply of milk was in great part produced in small dairies located within the city itself, or in the nearby suburbs, and sold by the producer from his own wagon as he made the daily rounds of his customers. Meat was also a local product, from animals killed in slaughter houses within the community and sold as soon as possible after slaughter.

A few foods had of course always come from distant sources; sugar, molasses, spices and condiments were articles of ocean commerce for centuries. The opening of the West moved the center of the nation's grain supply and of milling to west of the Mississippi. The preservation of fruits and vegetables by heating and sealing has a long history. The first experiments were made in France during the Napoleonic Wars, and actual industrial canning began in the United States in 1819. It was the perfection of this process that really began the revolution in food habits.

But with these exceptions, the mass of the food of our fathers and grandfathers was produced close to the place of its consumption and was subjected to the simplest and most necessary processing only.

We can, it is true, remember those early days without nostalgic longing for their return. The vegetables produced on nearby farms were not always of good quality and except for cabbage and turnips were available only for a brief season each year. The milk was dirty, of poor keeping quality and not infrequently dangerous. The meat was tough and stringy, and even its relative cheapness was not adequate consolation for its poor quality. Fruits were limited in amount and were, except for apples, available only for a short period each year. To those who lived in those parts of the country where cornbread was a staple diet, it is only the corn meal of the old days the disappearance of which is to be regretted.

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About the time when Benjamin Harrison became President of the United States, the tremendous increase in the population of the cities began to produce changes in the production and distribution of the food supplies of the nation. The invention of roller mills had made possible the production of flour of more agreeable appearance than was possible under older methods, and this flour rapidly drove from the market the product of the smaller local mills.

Similarly, the production of range cattle in the far West resulted in the establishment of great centers for the slaughter of cattle and in the development of methods for the shipment of meat and meat products to distant consumers. When "western beef," as it was called, was first introduced in the markets of the eastern cities, it was regarded with considerable disfavor. Consumers imagined that they could taste the preservatives which they wrongly believed had been used to make its shipment possible. In the beginning only its lower price commended it to the public.

The crowding of the cities made it impossible to continue to produce an adequate amount of milk within or near the city limits, and technologic methods were devised for shipping milk long distances. Successfully to manage this business required the creation of large corporations and the development of depots for collecting milk in rural areas and for distributing it in the cities. The use of refrigerated cars for the shipment of meat led quickly to the shipment of citrus fruits and vegetables in the same way. It was soon found profitable to raise each fruit or vegetable in that part of the country where climate and soil were most favorable to its production, and although market gardens near the cities have never quite disappeared, the great bulk of fruit and vegetable production was moved to areas far distant from the places of maximum consumption.

These changes were the inevitable result of the advances in horticulture, in food technology and in transportation, and without them the development of our present civilization could not have taken place. They brought, however, certain dangers to the health of the people, which made necessary the development of systems of protection of equal complexity. The most pressing were, of course, those connected with the production and distribution of milk. It was not difficult for the large corporations which engaged in the business of collecting and distributing milk to produce a product far cleaner and of better keeping quality than that coming from the neighborhood dairies of the past. However, the mingling of milk coming from many cows and its distribution by the larger companies to thousands or even hundreds of thousands of persons brought dangers which had previously not existed. The occasional infection of these large supplies of milk and milk products gave rise from time to time to epidemics involving thousands of cases of typhoid, scarlet fever and septic sore throat. The shipment of meat and of certain other products led to the use of preservatives, not all of which were entirely innocuous. The great commercial orchards and truck farms began to use insecticides in large quantities, and some of these were highly toxic and at least potentially dangerous to the health of those habitually using products in the growth of which these poisons had been employed.

The health departments of the nation reacted promptly and, in general, effectively to the challenge of these new conditions. The almost complete control of bovine tuberculosis, the inspection of all establishments where milk and its products were produced, distributed or sold and the enactment of ordinances requiring pasteurization of public milk supplies soon resulted in so safeguarding most of the nation's supply of milk that the dangers of wide distribution were almost completely controlled. The improved safety and quality resulted in a large increase in the consumption of milk, and a most significant contribution was thus made to the public health.

It was indeed fortunate that the federal government entered the field of food control soon after the beginning of this period of great change. Its first activities were in connection with meat inspection. Foreign countries threatened to interdict the shipment to them of American meat products, because of the fact that a large proportion of the pork shipped abroad at that time was found to be trichinous. It had not been deemed necessary to inspect pork products in the United States, since it was the habit in America to cook pork long enough to insure the destruction of trichinae. To meet this situation, the federal government established a system of inspection for meat slaughtered in the larger abattoirs of the country and destined for shipment overseas. It was not long before this inspection was extended to meat shipped interstate in the United States.

In the very first years of the twentieth century, Dr. Harvey W. Wiley, then the Chief of the Bureau of Chemistry of the United States Department of Agriculture, interested himself in the question of the adulteration of foods shipped in interstate commerce. Although Dr. Wiley was a man of extraordinary energy and courage, it was only after many years of effort that he succeeded in securing the passage of the Federal Food and Drug Act of 1906. The conditions which this act was designed to correct were not for the most part tremendously important by modern standards, but it was an exceedingly fortunate thing that the act itself was passed and that standards of purity and freedom from deleterious substances of our food supply were established and enforced by the federal government.

The passage of the federal act was followed, as is so often the case, by parallel legislation on the part of the states. Many of the state laws passed at this time, however, placed the enforcement of the whole system of food control in the hands of the department of agriculture rather than that of health. This fact, together with the long failure of the older city departments of health to develop adequate and effective systems of food inspection, gave food sanitation so low a position in the minds of the public health profession that it has even now not received the recognition it deserves. The demonstration about this same time of the tremendous importance of the accessory food factors in the nutrition of human beings and domestic animals and the widespread popularization of the facts have tended still more to obscure the importance of continuous, complete and effective control of all those foodstuffs which are processed in any way before reaching the ultimate consumer.

There is certainly no need in this company to review the arguments for an improvement in the diet of our people. The new knowledge of the importance of vitamins and of certain mineral substances to health and physical vigor is now known to all intelligent persons in every civilized country. The task remaining is to apply this knowledge to those who have not yet

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been reached by the flood of propaganda on the subject which has been poured forth in recent years. The success of the British government in maintaining the health of its whole people and in actually improving the physical status of its children during the late war, in the face of serious shortages of many foods, is proof positive of the need for the better utilization of the abundant food supplies of this country and in particular of the enormous importance of insuring to every expectant mother and every growing child a diet which in amount and content will make possible the fullest and most healthful development. This is the unfinished task in nutrition.

There are still, however, unfinished tasks in connection with the safety and sanitary quality of our food supply. The war waged by our growers of foods of all sorts on their insect enemies is never won, and it will probably continue as long as there are both human beings and insects on this little planet. Modern transportation is being utilized as well by the insect as by the human population of the earth, and new pests are constantly appearing in areas where they had not before been known. In this war, new weapons are constantly being developed and the old weapons are used in steadily increasing amounts. It was not very many years ago that arsenic began to be used as a spray for apples. The danger that the average citizen would receive a toxic amount of arsenic was not at first sufficiently serious to give rise to much concern. Since this early beginning, however, it has proved necessary to use arsenic in the commercial production of one after another of our fruits and vegetables, and the danger to the consumer is thus constantly increasing. It seems probable that insecticides free from toxicity to human beings will in time replace the present dangerous substances. It will always be necessary, however, for the health department to protect the interests of the individual consumer who has no means of knowing the danger to which he is subjected and is always poorly represented when any question of legislation is under consideration.

When the replacement of the original Federal Food and Drugs Act by what is now called the Federal Food, Drug and Cosmetic Act was pending before the Congress of the United States, the interests of the public were presented to the committee by the representative of the Federal Food and Drug Administration, whose motives were plainly suspect of the committee, and by the three physicians who were called "the three professors," who appeared voluntarily as witnesses in behalf of the bill. In opposition were several hundred lawyers, lobbyists and technicians of the various food-producing and processing interests involved. Each one of these paid lobbyists was fully aware of the effect of the bill on the interests of his own client and was prepared to expend all the time, energy and money necessary to protect those interests. No administrative health officer appeared at these hearings.

What has been said about insecticides applies equally to a wide variety of other chemical substances which have been developed and which are now being used in the processing of food on a commercial scale. Until Mellanby's demonstration of the fact that flour treated with nitrogen trichloride, the so-called "agene," produced hysteria in dogs, few if any even of our best informed health officers were aware of the fact that a large proportion of all flour now sold on the American market is treated with this powerful chemical agent. There is as yet, of course, no evidence that the "agenizing" of flour has produced any ill effects on our human population, but Mellanby's observations have been confirmed and extended in this country, and no one as yet knows the effect on human beings of the prolonged and regular use of "agenized" flour, or whether or not there will be remote and serious results from its occasional use by so large a part of the population.

"Agene" is very much in the limelight at the moment, but it is by no means the only substance used in this country in the processing of flour. Chlorine, nitrosyl chloride, benzoyl peroxide and the oxides of nitrogen are all used for bleaching flour and for additional aging effect. Potassium bromate is used as a conditioner, to make the flour easier to handle and to produce loaves of greater volume than is possible without the addition of this agent. Sodium bicarbonate, calcium phosphate and sodium acid pyrophosphate are also added to certain flours to produce one or another effect.

In the processing of evaporated milk, disodium phosphate, sodium citrate and calcium chloride are used as stabilizers. In the making of cream cheeses, gum karaya, gum tragacanth, carob bean gum, gelatin and algin are used to prevent the leakage of moisture from the product. In the making of preserves, jams and jellies, lactic, malic and tartaric acids are used to increase the acidity of the product and sodium citrate and potassium tartrate are used as buffer salts to prevent its too rapid jelling. This list of products now regularly in such use could be extended to great length, and, in addition, a large number of new products are now being used experimentally. It should be made clear that up to this time there is no evidence that any of these substances is known unfavorably to affect the health of consumers of the product. The Food and Drug Administration has actively interested itself in the subject and has formulated stringent regulations for controlling the use of all such substances.

Surely it would seem that this situation should be a source of concern to every state and local health officer in this country and that the efforts of the federal government to control it should be aided and encouraged in every possible way. When it is proposed to use a new substance of this kind, the representatives of the food industry are at once mobilized and every possible scrap of evidence in favor of the use of the product is assembled and presented to the official agency. The millions of consumers whose health is placed in possible danger have no knowledge of the fact that their interests are in jeopardy and no means by which these interests can be represented. This important field deserves far more attention at the hands of all health officers than it has up to now received.

The nation's food is more than ever, therefore, the concern and responsibility of our health officials. Its control has passed far beyond the condemning of spoiled meats, fruits and vegetables and making perfunctory inspections of restaurants. These classic functions must, of course, continue to be performed and should be done as well as our existing facilities make possible. There is, however, another and higher duty which we must recognize and another responsibility we must assume, and that is to make sure that in the enormous business of producing, processing and distributing the food supply of our great population, the interest of the consumer and particularly the health of the consumer must always come before the convenience or the profit of those who supply it.

METHODS OF PROTECTION AGAINST HOMOLOGOUS SERUM HEPATITIS

I. Studies on the Protective Value of Gamma Globulin in Homologous Serum Hepatitis SH Virus

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Antigenic differences between certain strains of infectious (epidemic) hepatitis virus (IH) of relatively short incubation (about eighteen to forty days) and certain strains of serum hepatitis virus (SH) of relatively long incubation (about sixty to one hundred and fifty days)[1] have been conclusively demonstrated. The data of Oliphant,[2] suggesting immunologic similarities in such viruses, could well be explained by the facts that: (1) the virus, designated by Oliphant as that of epidemic hepatitis, had a long incubation period (about seventy-five days), (2) thus, it actually may have been a strain of serum hepatitis virus, SH, rather than one of epidemic hepatitis, IH, and (3) a cross immunity with his designated serum hepatitis virus, SH, therefore would not have been surprising.

The confusion concerning the origin of such strains of hepatitis virus can best be clarified by study of their immunologic behavior in experimental subjects. It thus would appear important from the viewpoint of experimental studies that virus agents in infective materials should be only tentatively designated by the term "infectious hepatitis" (IH) or "serum hepatitis" (SH) until the immunologic and other properties of the agent concerned have been demonstrated. When these properties are not known, reference to the disease as "viral hepatitis" might avoid the classification of a virus as one of "infectious hepatitis" (IH), when later it may prove to be one of the strains of "serum hepatitis virus" (SH). The existence of such confusion is evident from the experimentally demonstrated presence of both strains of virus in the blood, although the serum hepatitis virus (SH) has not been obtained from the commonly infective source of the infectious (epidemic) hepatitis virus (IH); i. e., the stool. The data of the present report, although not adding conclusive evidence for or against the antigenic differences already demonstrated, have pointed to an interesting difference between them in respect to the protective effect of gamma globulin.

These data have indicated not only a differing effect on serum hepatitis SH with different batches of gamma globulin, but also an interesting phenomenon in the field of viral diseases, namely, an apparent prolongation of the incubation period of serum hepatitis SH by the parenteral injection of certain batches of gamma globulin, 10 cc., during this period. In contrast, in the studies to date on infectious (epidemic) hepatitis IH, such prolongation apparently has not been observed.

GAMMA GLOBULIN IN INFECTIOUS (EPIDEMIC) HEPATITIS (IH VIRUS)

The use of gamma globulin obtained from large pools of American Red Cross blood by means of the fractionation method developed by Cohn and his co-workers in the prevention of hepatitis IH has been previously described.[3] In four epidemics of hepatitis IH in widely separated areas, gamma globulin in amounts of approximately 0.06 to 0.15 cc. per pound of body weight was effective in protecting a large proportion of exposed susceptible persons. In the first epidemic in which gamma globulin was used prophylactically, attenuation of the disease was observed in a number of persons who were not completely protected.[3a] In these persons and in the few in whom unmodified hepatitis developed, despite previous injection of gamma globulin, no prolongation of the incubation period was apparent, although the evidence on this point was inconclusive because of the uncertainty of the exact time of exposure. However, if prolongation of the incubation period had occurred, a number of cases of hepatitis should have been noted in the treated group more than one week after the injection of the globulin. The paucity of such cases suggests that in this disease the globulin usually either prevented or attenuated the disease, without apparent prolongation of the incubation period.

Confirmatory evidence for such protection and attenuation, together with absence of prolongation of the incubation period, was obtained by Paul and Havens in a similar study.[4] In this study also, the lack of cases occurring more than ten days after the injection of the globulin apparently indicated that the incubation period had not been lengthened by the parenteral injection of the globulin.

In the two epidemics of hepatitis IH in the Mediterranean Theater of Operations in which gamma globulin was used prophylactically, it was not possible to obtain data relative to attenuation of hepatitis or to prolongation of the incubation period.[3b]

GAMMA GLOBULIN IN HEPATITIS SH

Field Studies.—The study of the effect of prophylactic gamma globulin on hepatitis SH (long incubation period) has been hampered by the lack of clearcut epidemics of the disease. The groups studied to date have been composed entirely of battle casualties who had received transfusions of blood or plasma in the various theaters of operation and then had been evacuated to general hospitals in the Zone of the Interior. That the hepatitis which occurred in these groups was, in almost all instances, hepatitis SH was indicated by the fact that in other battle casualties in the same hospitals who had not received blood products hepatitis rarely developed, and the incubation period apparently in all cases was more than sixty days. Studies have been reported in two different groups of such battle casualties in two widely separated United States Army general

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These investigations were conducted in part under the Commissions on Measles and Mumps, on Virus and Rickettsial Diseases, and on Liver Disease, Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, United States Army, Washington, D. C.

1. Neefe, J. R.; Stokes, J., Jr., and Gellis, S. S.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis: Experimental Study of Immunity and Cross-Immunity in Volunteers: A Preliminary Report, Am. J. M. Sc. **210**: 561, 1945. Neefe, J. R.; Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis: Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents, Am. J. Med. **1**: 3 (July) 1946.

2. Oliphant, J. W.: Infectious Hepatitis: Experimental Study of Immunity, Pub. Health Rep. **59**: 1614, 1944.

3. (a) Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, J. A. M. A. **127**: 144 (Jan. 20) 1945. (b) Gellis, S. S.; Stokes, J., Jr.; Brother, G. M.; Hall, W. M.; Gilmore, H. R.; Beyer, E., and Morrissey, R. A.: The Use of Human Immune Serum Globulin (Gamma Globulin) in Infectious (Epidemic) Hepatitis in the Mediterranean Theatre of Operations: I. Studies on Prophylaxis in Two Epidemics of Infectious Hepatitis, J. A. M. A. **128**: 1062 (Aug. 18) 1945.

4. Havens, W. P., Jr., and Paul, J. R.: Prevention of Infectious Hepatitis with Gamma Globulin, J. A. M. A. **129**: 270 (Sept. 22) 1945.

hospitals.[5] In the first hospital, two doses of gamma globulin of 10 cc. each were injected at an interval of thirty days in alternate battle casualties who had received blood or plasma following injury. That the test and control groups were chosen by chance is indicated by the closely similar distribution of the battle casualties from the Mediterranean, European and Pacific theaters of operation in these two groups. In this controlled study excellent protection apparently was afforded against the hepatitis SH virus by the gamma globulin. However, in the second study, at the other hospital, in which a single dose of gamma globulin, 10 cc., was used, there was no significant difference in incidence of hepatitis SH noted between the test and control groups. Despite the lack of complete protection, the group data indicated that the single injection of gamma globulin had resulted in a prolongation of the mean incubation period. While the mean length of time between transfusion and injection of globulin in the test group was almost identical with the mean length of time between transfusion and the day of designation as a control in the other (control) group, the succeeding mean intervals to the onset of hepatitis were different. In the test group the interval (fifty-two days) was over 50 per cent longer than the comparable interval (thirty-four days) in the controls. As the possibility was approximately 1 in 400 that such a prolongation was purely the result of chance, the observations suggest the presence of a virus-inhibiting factor in the batch of gamma globulin used, in spite of its lack of effect on the incidence of the disease.

TABLE 1.—*Tabulation of Data from McGuire General Hospital**

Interval † in Two Week Periods	Number of Patients Given Globulin	Number of Patients Not Given Globulin
0	..	..
2	..	..
4	..	..
6	1	4
8	3	7
10	2	8
12	4	5
14	4	4
16	4	3
18	3	..
20	5	..
22	3	..
24	4	..
26 and over	12	2
Total	41	33

* These data were furnished by Major William A. Jeffers, Medical Corps, Army of the United States, and Major Philip E. Bartwell, Medical Corps, Army of the United States.

† Intervals from transfusion to onset of hepatitis in 76 patients who had previously received transfusions and who subsequently had hepatitis. The mean interval for patients given globulin was one hundred and sixty-one days and the mean interval for patients not given globulin eighty-eight days.

As a result of the protective effect indicated by the decrease incidence of hepatitis SH in those given injections at the first hospital, all Army general hospitals in this country were directed to administer routinely, on admission, a single intramuscular injection of gamma globulin to all newly evacuated battle casualties that had received transfusions. For this reason, further comparative studies with casualties (not given injections) as controls were not possible. In one hospital, however, carefully collected data permitted a comparison between the mean incubation period of cases of hepatitis which preceded the routine use of globulin and the mean incubation period of cases which occurred after the routine single injections of gamma globulin were started. As the control period preceding the routine use of gamma globulin was approximately five months in duration, whereas the study period following institution of the routine use of globulin was approximately seven months, the time intervals are not comparable. However, the case rate of hepatitis in battle casualties that had received transfusions in this hospital remained approximately the same throughout this twelve month period.[6] Thus, the occurrence of 33 cases of hepatitis in the control group and of 43 cases in the group given injections within the five and seven month periods, respectively, would approximate the expected number if there were no decided change in the case rate. This suggested that the single dose of globulin, 10 cc., had not decreased the incidence of hepatitis SH. That 3 deaths occurred in the 33 control casualties, whereas no deaths occurred in the groups given injections, is of interest, although not statistically significant. Although ineffective in decreasing the incidence, a highly significant difference was observed between the mean incubation period (eighty-eight days) in casualties not treated with gamma globulin and the mean incubation period (one hundred and sixty-one days) in the casualties treated with gamma globulin. These data are presented in table 1. As in the second hospital previously mentioned, the observations in this third hospital also strongly suggested some inhibitory effect of the batch of globulin used on the virus of hepatitis SH.

TABLE 2.—*Effect of Gamma Globulin on Hepatitis Virus SH (Experimentally Induced Hepatitis): Study No. 1*

Material Injected	Number of Volunteers	Results: Hepatitis With Jaundice	Results: Hepatitis Without Jaundice	Incubation (Days)
2 cc. infective plasma	4	2	0	101; 112
Mixture: 2 cc. infective plasma, 1 cc. gamma globulin	5	2	1	105; 117; 138
2 cc. infective plasma, 10 cc. gamma globulin simultaneously at separate sites	3	1	1	108; 112

TABLE 3.—*Effect of Gamma Globulin on Hepatitis Virus SH (Experimentally Induced Hepatitis): Study No. 2*

Material Injected	Number of Volunteers	Presumptive Cases	Hepatitis Without Jaundice	Incubation (Days)
3 cc. infective plasma	7	2	2	62; 94 70; 73
Mixture: 3 cc. infective plasma, 10 cc. gamma globulin	7	2	1	80; 98 73
3 cc. infective plasma, followed by 10 cc. gamma globulin after 1, 2 and 3 mo.	7	0	0	.....

5. Grossman, E. B.; Stewart, S. G., and Stokes, J., Jr.: Post Transfusion Hepatitis in Battle Casualties, J. A. M. A. **129**:991 (Dec. 8) 1945. Duncan, G.; Christian, H. A.; Stokes, J., Jr.; Rezer, W. F.; Nicholson, J. T., and Edgar, A.: An Evaluation of Immune Serum Globulin as a Prophylactic Agent Against Homologous Serum Hepatitis, Am. J. Med. Sc. **213**:53 (Jan.) 1947.

6. Personal communication to the authors from Major William A. Jeffers, Medical Corps, Army of the United States, Chief of Medical Service, McGuire General Hospital, Richmond, Va. The incubation periods were calculated from the date of injury, although plasma or blood, injected also on subsequent dates, might have been responsible for the hepatitis. Such errors should have occurred with approximately equal frequency in the control and treated groups and, thus, would not alter essentially the evidence obtained of decided differences between the groups.

GAMMA GLOBULIN IN EXPERIMENTALLY INDUCED HEPATITIS SH

Studies were carried out to determine the possible protective effect of gamma globulin against the hepatitis virus SH [1, 2] in volunteers.

In the first study, 5 volunteers each received parenteral injections of a mixture composed of 2 cc. of icterogenic plasma (virus SH) and 1 cc. of human immune serum (gamma) globulin. In 3 of these volunteers hepatitis developed, in 2 with jaundice and in 1 without jaundice. Five other volunteers simultaneously received, at separate sites of injection, 2 cc. of the icterogenic plasma and 10 cc. of the gamma globulin preparation. In 2 of these volunteers hepatitis developed, in 1 with jaundice and in 1 without jaundice. Of 4 control volunteers who received parenterally the icterogenic plasma alone, in 2 hepatitis with jaundice developed. The results are summarized in table 2. No significant differences in the lengths of the incubation periods were observed in the cases in these different groups, the interval between injection and the onset of hepatitis being three to three and a half months in all.

TABLE 4.—*Effect of Gamma Globulin on Hepatitis Virus SH (Experimentally Induced Hepatitis): Study No. 3*

Material Infected	Number of Volunteers	Results: Hepatitis With Jaundice	Results: Hepatitis Without Jaundice	Results: Questionable Hepatitis	Incubation (Days)
1 cc. infective serum	7	1	1	2	66; 66; 102; 72
Mixture: 1 cc. infective serum, 20 cc. gamma globulin	7	2	1	0	65; 109; 73
1 cc. infective serum followed by gamma globulin, 0.06 cc. per pound of body weight after 1, 2 and 3 mo.	7	2	1	1	82; 70; 68; 80

The third study was similar to the second. The same strain of hepatitis virus SH was used, but the material represented the second human passage virus SH (Fort Bragg strain). Seven volunteers were each given intramuscular injections of a mixture composed of 1 cc. of icterogenic serum and 20 cc. of gamma globulin. In 2 of the volunteers hepatitis developed with jaundice, and in 1 hepatitis developed without jaundice. Seven other volunteers simultaneously received by intramuscular injection 1 cc. of the icterogenic serum, followed by an injection of gamma globulin, 0.06 cc. per pound of body weight, after one, two and three months, respectively. In 2 of the volunteers hepatitis with jaundice developed; 1 had hepatitis without jaundice, and 1 had questionable hepatitis. Seven volunteers served as controls. Each received intramuscularly 1 cc. of icterogenic serum. In 1 of the volunteers hepatitis developed with jaundice; 1 had hepatitis without jaundice, and 2 had questionable hepatitis. The results are summarized in table 4. Gamma globulin afforded no protection either when mixed with virus SH previous to injection or in evidence of hepatitis. Seven volunteers served as controls. Each received intramuscularly 3 cc. of icterogenic plasma. In 2 of these volunteers mild hepatitis developed without jaundice, and 2 had questionable hepatitis. The results are summarized in table 3. Since only mild hepatitis without jaundice was produced in the group of controls, it seemed probable that the viral agent had become attenuated. Therefore, the apparent protection afforded by three 10 cc. doses of gamma globulin against this attenuated agent must be regarded as inconclusive. On the other hand, the preparation of gamma globulin used failed to neutralize the attenuated viral agent. This is indicated by a similar incidence and similar incubation period of mild hepatitis in the group receiving the neutralization mixture and in the group of controls.

TABLE 5.—*Effect of Convalescent Plasma on Hepatitis Virus SH*

Group	Material and Amount	Number Inoculated	Results: Hepatitis With Jaundice	Results: Hepatitis Without Jaundice	Results: Percentage of Hepatitis	Incubation (Days)
Test	Mixture: 2 cc. infective serum, 10 cc. convalescent plasma followed by 20 cc. convalescent plasma after 1, 2 and 3 mo.	4	1	0	25	98
Control	10 cc. convalescent plasma	4	0	0	0.0	..

The clinical study in one of the United States Army general hospitals already mentioned indicated a significant decrease in the incidence of hepatitis SH among the group of battle casualties receiving two doses of gamma globulin of 10 cc. each at an interval of thirty days. The second and third studies were carried out to ascertain the value of three prophylactic doses of gamma globulin against hepatitis virus SH and to study further the neutralizing effect of gamma globulin on this virus.

In the second study, 7 volunteers were each given intramuscular injections of a mixture composed of 3 cc. of icterogenic plasma and 10 cc. of gamma globulin. In 1 of these volunteers mild hepatitis developed without jaundice, and 2 had questionable hepatitis. Each of 7 other volunteers simultaneously received by injection 3 cc. of icterogenic plasma, followed by 10 cc. of gamma globulin after one, two and three months, respectively. None of these volunteers showed any multiple prophylactic doses injected at later intervals. No significant difference in the length of the incubation period was observed in these different groups.

CONVALESCENT PLASMA IN EXPERIMENTALLY INDUCED HEPATITIS SH

Study No. 4.—A study was carried out of the possible protective effect of hepatitis convalescent plasma against hepatitis virus SH. The same icterogenic serum (Fort Bragg virus, second passage) used in the last gamma globulin study was employed. The convalescent plasma was obtained from a single case of hepatitis SH with jaundice two and one-half months after recovery.

Four volunteers were each given intramuscular injections of a mixture composed of 2 cc. of icterogenic serum and 10 cc. of convalescent plasma, followed by 20 cc. of convalescent plasma after one, two and three months, respectively. In 1 of the volunteers hepatitis

with jaundice developed. In order to determine whether or not the convalescent plasma contained hepatitis virus SH, 4 volunteers were given parenteral injections of the convalescent plasma alone. None showed evidence of hepatitis. The results are summarized in table 5. In this study, which was too limited for conclusive evidence, convalescent plasma from a single person apparently failed to protect against hepatitis virus SH, suggesting that neutralizing antibodies were either absent or not present in sufficient concentration to afford protection.

COMMENT

The significance of the aforementioned observations may be reviewed in the light of the following considerations:

1. The Possible Inhibiting Effect of Gamma Globulin on Different Strains of Hepatitis Virus.—There can be little question that various batches of gamma globulin prepared from pools of plasma from two to three thousand donors, collected during World War II by the American Red Cross, have had a decidedly inhibiting effect on the virus of the infectious (epidemic) hepatitis IH, in view of the protective results obtained in the four widely separated epidemics mentioned. Although no direct neutralization studies utilizing the globulin and strains of this virus have been carried out, it appears highly probable that the resistance of the human host results from the passive transfer of protective antibodies in the gamma globulin. Despite the lack of measurement of such antibodies, it also appears probable, inasmuch as various batches of globulin have been effective, that a fairly uniform titer of such antibodies has been present. Such uniformity would be entirely similar to the fairly uniform titers in gamma globulin of other virus antibodies, such as those of human influenza viruses A and B and of swine influenza virus. If present, such general uniformity could accord with a wide prevalence of infectious hepatitis IH in an apparent (clinical) or in an inapparent (subclinical) form. The epidemiologic studies of this disease, particularly as related to the frequency of the virus in the stools, could well explain its wide prevalence in the general population in the apparent or inapparent forms, with a resulting antibody production.

The field observations on serum hepatitis SH have included studies in three widely separated general hospitals in which large amounts and different batches of gamma globulin were used. In all three studies, the gamma globulin appeared to have an inhibiting effect on the virus. The effect was protective, however, only in the study in which two doses of 10 cc. each were used.

In the studies on volunteers, it is possible that the strain of virus was different from that (or those) encountered in the battle casualties. Differences in the quantity or composition of the gamma globulin preparations also may account for the lack of protection, since it is possible that hepatitis virus SH is not as widespread as virus IH or does not produce sufficient neutralizing antibodies to be protective even when concentrated. The fractionation process or storage of gamma globulin may have diminished or destroyed antibodies present in the original plasma, although in all batches used satisfactory titers of antibodies against influenza A and B viruses were observed. (For influenza A virus, the PR 8 strain was used; for influenza B virus, the Lee strain was used.)

In the study with volunteers in which a neutralization test was carried out with hepatitis SH convalescent plasma, and multiple prophylactic doses of convalescent plasma were subsequently injected, virus-neutralizing antibodies could not be demonstrated. This convalescent plasma was taken from one patient having hepatitis with jaundice as a result of inoculation with the same strain of hepatitis virus SH used in this study. Because of the small size of the group, no conclusions can be drawn.

Despite the many problems which remain unanswered, these studies seem to afford some additional evidence for antigenic differences between hepatitis viruses SH (Fort Bragg strain) and the epidemic IH strains previously studied. The final solution of this problem and the evaluation of the role of gamma globulin in the prophylaxis of serum hepatitis obviously will require further studies in volunteers or, should they become available, in susceptible animals.

As little is known of the epidemiologic aspects of serum virus SH hepatitis, which may possibly be different from that of infectious (epidemic) hepatitis, a hypothetic discussion concerning the incidence of apparent or inapparent cases is not appropriate. Certain evidence suggests that human carrier states may exist wherein the virus of serum hepatitis is present either continuously or from time to time in the blood stream, in such form as to infect recipients of whole blood or plasma from donors who may act as "carriers." In what manner gamma globulin from large pools of plasma could acquire virus-inhibiting properties against such a virus agent is highly speculative and beyond the scope of this discusson.

2. The Possible Presence of Active Serum Hepatitis Virus in Gamma Globulin.—The question arose as to whether the recorded delay in the incubation period of serum hepatitis in the hospitals studied did not result from the presence of the active serum hepatitis virus in the injected gamma globulin. If present and active, this could have caused a later increase of serum hepatitis in the groups given injections and, in the case of the last hospital, could partly have accounted for the exceptional length of the mean incubation period in the group given injections. That the presence of active virus in the gamma globulin would not explain the recorded observations appears clear for the following reasons: (*a*) At the first hospital, the two doses of globulin, given one month apart, apparently afforded a high degree of protection, and cases of hepatitis in the test group did not continue to appear, as should have been the case if the gamma globulin had been infective. (*b*) At the second hospital, the incidences of hepatitis in the test and control groups, chosen alternately, were not significantly different. The test group should have shown a significantly higher incidence of hepatitis, rather than merely a prolonged mean incubation period, if the gamma globulin itself had been infective. (*c*) At the third hospital, although it lacked the alternation of choice of test and control groups, the similar incidence of hepatitis both preceding and following the use of gamma globulin indicated that the globulin itself had not been infective. (*d*) Finally, serum hepatitis has not been observed in children given injections of gamma globulin for prophylaxis against other diseases. In studies on measles, approxi-

mately 3,000 children thus treated have been followed up carefully, with complete absence of any evidence that active serum hepatitis virus was present in the gamma globulin used. The absence of hepatitis in so large a number of the susceptible subjects (children) that received injections appears highly significant.[7]

Enders [8] has observed that when mouse encephalomyelitis virus (Theiler's virus) and tobacco mosaic virus were added to pools of plasma in which no antibodies to these viruses were present, the gamma globulin fractions, as well as all other fractions of the plasma obtained by the method of Cohn and his co-workers, still contained the active viruses. The strains of virus of serum hepatitis thus far studied appear to be comparatively resistant to heat and to other treatment, so that the process of fractionation presumably should not inactivate them if they behaved in a manner at all similar to that of the other two viruses mentioned. The apparent absence of active serum hepatitis virus from the gamma globulin fractions thus far studied may result from inhibiting or neutralizing factors present at times in the large pools of plasma of the American Red Cross, from which the gamma globulin used in these studies was derived. It is also possible that the concentration of such inhibiting or neutralizing factors in the gamma globulin may add to both the safety and effectiveness of such materials. It seems possible that a few persons with extremely high titers of antibodies to the virus of serum hepatitis may furnish a protective titer for the entire pool and, in particular, for certain batches of the gamma globulin derived from such pools.

However, cases of hepatitis reported to the American Red Cross [9] among persons receiving fraction I (fibrinogen and antihemophilic globulins) indicate the frequent presence of virus SH in this fraction. Its apparent absence from the gamma globulin of fractions II and III and the absence of virus SH antibodies from many batches studied of these same fractions necessitate consideration of the following possibilities.

1. The virus SH may differ from the animal and plant viruses studied by Enders [8] in its distribution among the fractions and may be concentrated in fraction I, possibly as the result of affinity for certain proteins.

2. The virus SH may form complexes with proteins in fractions II and III, which are filtered out or lost during processing.

3. The virus SH may be inactivated under the conditions of storage and handling of gamma globulin which have been more rigorous than those employed for fraction I.

The dilution factor discussed by Andrewes [10] in its possible relation to the occurrence of serum hepatitis cannot as yet be fully evaluated. It is thus clear that many of the problems here discussed concerning the epidemiologic study and control of serum hepatitis require additional basic data before conclusive answers to them can be found.

7. Three cases of supposedly long incubation hepatitis following gamma globulin therapy have been mentioned personally to the authors. All of these could possibly have been chance infections with the IH virus. The paucity of such occurrences, when compared with the relatively high incidence (5 to 7 per cent) following treatment with pooled plasma from which the gamma globulin was prepared, strongly suggests that the gamma globulin was not in itself responsible for such hepatitis.

8. Cited by Gellis, S. S.; Neefe, J. R.; Stokes, J., Jr.; Janeway, C. A., and Scatchard, G.: Chemical, Clinical, and Immunological Studies on the Products of Human Plasma Fractionation XXXVI: Inactivation of the Virus of Homologous Serum Hepatitis in Solutions of Normal Human Serum Albumin by Means of Heat, J. Clin. Investigation **27**: 239 (March) 1948.

9. Janeway, C. A.: Personal communication to the authors.

10. Andrewes, C. H.: Jaundice and the Dilution Phenomenon, editorial, Lancet **2**: 159, 1944.

3. The Possible Mode of Action of Gamma Globulin as Related to the Incubation Period of Serum Hepatitis.—Inasmuch as the evidence obtained from the three studies in the general hospitals suggests the presence of inhibiting factors in certain batches of gamma globulin against the serum hepatitis virus, it is of particular interest to consider the possible manner in which the injection of a single dose, 10 cc., of gamma globulin may prolong the incubation period. A moderate amount of clinical evidence indicates that convalescent mumps plasma, given in sufficient quantities parenterally, at times will lengthen the incubation period of this disease but will rarely protect completely the exposed susceptible person. Such behavior appears to be rare in viral diseases. In serum hepatitis, the length of the incubation period may indicate a balanced relation between parasite and host which lends itself to effective inhibition or lengthening of the incubation period of the parasite by a relatively small amount of inhibiting factor. The effect of the gamma globulin may be based on a purely quantitative relation between the number of viral bodies and the amount of inhibiting factor in the gamma globulin. Thus, two doses of 10 cc. given at a thirty day interval, or 20 cc. in all, may be sufficient to neutralize all of the virus particles present, whereas one dose, 10 cc., may reduce the amount of virus to a point from which the relatively slow process of multiplication is repeated. Thus, the prolongation of the incubation period may be solely the result of delay in the parasite's increase of virus particles to a point at which clinical disease can be developed.

On the other hand, the protective effect of the two doses of gamma globulin may have resulted from the fact that the second injection of antibodies had occurred at a more vulnerable step in the life cycle of the parasite, possibly when it was present in the blood stream and before extensive cellular invasion had occurred. In lieu of further evidence, it would appear that the first and simpler hypothesis is the more tenable.

SUMMARY AND CONCLUSIONS

Gamma globulin from large pools of human plasma apparently contains protective factors against strains of infectious (epidemic) hepatitis IH virus of shorter incubation (approximately eighteen to forty days). Gamma globulin also has shown decided differences in its protective properties against strains of serum hepatitis SH virus of longer incubation (approximately sixty to one hundred and fifty days). In the infectious (epidemic) hepatitis IH, the protective effect has been conclusively demonstrated. In serum hepatitis SH at one general hospital for battle casualties, two injections of gamma globulin, 10 cc. each, given at a thirty day interval during the incubation period of the disease, were highly protective. In two other general hospitals, in which a single injection of gamma globulin (10 cc.) was administered during the incubation period, decided prolongation of the mean incubation periods resulted in the two test groups of battle casualties. In these two hospitals, the gamma globulin apparently did not alter the incidence of hepatitis SH in the test groups, despite its prolongation of the mean incubation periods. Four deaths occurred in the control groups and none in the groups given injections in these two hospitals.

In contrast to serum hepatitis SH, prolongation of the incubation period as the result of previous injection of gamma globulin has not been observed in infectious (epidemic) hepatitis IH, the effect being one of protection or attenuation.

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In a group of studies in volunteers, the batches of gamma globulin tested apparently did not contain virus-neutralizing or inhibiting factors effective against the strain of serum hepatitis SH virus used. In a single small study, hepatitis convalescent plasma from one subject failed to afford inhibiting factors against the same strain of serum hepatitis SH virus.

It appears possible that the process of fractionation itself may concentrate the virus in fractions other than the gamma globulin or that the manipulations of filtering and storage may eliminate the virus, while in certain batches of gamma globulin protective antibodies may be an added factor in preventing contamination of the gamma globulin with virus SH.

NOTE.—It was found impossible to trace each source of plasma for the gamma globulin used in these studies. Gamma globulin for the volunteer studies consisted of material derived from more than one biologic firm and from several areas of the United States. It included both fraction II and III-1 gamma globulin, in the proportions they are obtained in the most recent method developed by Oncley and his associates for the subfractionation of II and III. These were lots number 14, 28-4, 33-1, 68-2 and 68-3.

METHODS OF PROTECTION AGAINST HOMOLOGOUS SERUM HEPATITIS

II. The Inactivation of Hepatitis Virus SH with Ultraviolet Rays

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Much attention has been focused on the transmission of the causative agent of homologous serum hepatitis by the parenteral administration of blood and blood products. A number of conclusive experimental studies have shown that plasma and serum may harbor the responsible viral agent.[1] During the recent war, in many battle casualties who had received transfusions of whole blood or plasma, or both, subsequently, within periods of two to five months, homologous serum hepatitis developed.[2] Since the end of the war and the release of large stores of dried pooled plasma for civilian use in this country, a significantly high incidence of serum hepatitis has been reported resulting from transfusions with this and other plasma.[3] Reports from England by Spurling, Shone and Vaughan[4] also indicate an incidence of 7.3 per cent homologous serum jaundice among 1,054 patients receiving pooled serum and plasma. Inasmuch as laboratory methods for the detection of icterogenic agents in blood and blood products have not been perfected, the prevention of homologous serum hepatitis has offered a challenge to investigators in the field of preventive medicine.

Methods of control of homologous serum hepatitis, thus far, have been inadequate. Careful selection of donors has been helpful. However, this latter method does not exclude those persons who might have had inapparent infections and possibly remained as carriers and those persons whose blood might be obtained during the long incubation period of the disease.

A means for inactivating hepatitis virus SH [1b] in serum albumin by prolonged heating has been demonstrated.[5] This method, however, is not applicable to whole blood, plasma or serum. Recent experimental studies have shown human immune (gamma) globulin to be unreliable in providing protective antibodies.[6]

The inactivation of other viruses by exposure to ultraviolet rays has been successfully employed by many investigators. The Oppenheimer-Levinson apparatus[7] and the Habel-Sockrider apparatus,[8] both utilizing the general principle of irradiating continuously flowing thin films of virus suspensions, have demonstrated the usefulness of these methods under certain conditions.

The possibility of inactivating hepatitis virus SH in plasma and serum has been investigated to a limited extent, but, thus far, the results of these studies have been conflicting. In this country, the work of Oliphant suggested that hepatitis virus SH in serum could be inactivated with ultraviolet rays.[9] However, in his series of studies, there was wide variation in the amounts of radiant energy used. Also, the effect of irradiation on the serum proteins apparently was not fully determined. In England, MacCallum and his co-workers carried out similar studies.[10] Results contrary to those of Oliphant were obtained, inasmuch as the supposedly suitable exposure failed to inactivate the viral agent. Where greater exposure was used, gross changes in the serum proteins were noted in electrophoretic studies.

The recent work of Wolf and his co-workers, with the Oppenheimer-Levinson apparatus, suggested that plasma may be irradiated without significant alteration of the proteins and safely administered to patients.[11] Their work did not involve the use of hepatitis viral agents.

The purpose of this paper is to present experimental evidence indicating that hepatitis virus SH (homologous

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serum jaundice) can be inactivated with ultraviolet rays and that such inactivation may be accomplished by a safe and practical procedure.

METHODS AND MATERIALS

Source and Nature of Materials.—The icterogenic material used in this study represented a pool of serum specimens collected from volunteers during the early stages of induced homologous serum hepatitis. This serum had been continuously frozen at —20 C. for a period of two and one-half years. The strain of virus SH contained in this serum has been described in previous reports.[1a] One lot of this serum pool, when used six months prior to the present study, produced hepatitis in approximately 50 per cent of the inoculated volunteers.[5]

Volunteers.—Healthy adult male volunteers were used in this study. Preliminary data prior to their inoculation have been dealt with in a previous report.[1a] Preinoculation hepatic studies were performed on each volunteer to rule out the possibility of asymptomatic hepatic disease and to establish for each subject a range of normal values for the various hepatic tests.

Ultraviolet Apparatus.—A Habel-Sockrider type of apparatus was used for processing the icterogenic serum.[6] This apparatus consisted of a rotating glass tube, 52 cm. in length and 2.53 cm. in diameter. An 18 watt cold quartz lamp [12] passed lengthwise through the center of the glass tube. This lamp has an intensity of about 3,500 microwatts per square centimeter at a distance of 9 mm., which was the distance from the burner to the surface of the serum irradiated in the rotating tube. Approximately 85 per cent of its radiation is given off in the 2,537 angstrom unit wavelength. The glass tube could be rotated at varying speeds. For the present experiment 240 revolutions per minute were used, with the glass tube at an angle of 12 degrees from the horizontal.

Procedure.—The icterogenic serum was thawed and then screened through sterile 200 mesh silk to remove flocculent material. The serum was delivered from a separatory funnel to the side of the rotating tube at a constant rate of flow controlled by a flow meter. The rate of flow was 24 cc. per minute, and the time of exposure was 10 seconds. The average thickness of the film of serum was calculated to be 0.263 mm. Turbulence produced by rotation resulted in a similar exposure to irradiation of all parts of the serum.

Inoculations.—A group of 15 volunteers served as controls and received portions of the same icterogenic serum without irradiation by intramuscular injection. Of this group of 15, 11 volunteers each received 4 cc. of icterogenic nonirradiated serum. Of the remaining 4 volunteers, each received a mixture composed of 2 cc. of icterogenic nonirradiated serum and 10 cc. of plasma from 1 subject, convalescent two and a half months. Each subject also received 20 cc. of the same convalescent plasma after one, two and three months, respectively. This latter group of 4 was controlled by a second group of 4 volunteers, each of whom received 10 cc. of the same convalescent plasma in a single dose. This latter group was arranged for the purpose of determining whether the convalescent plasma harbored active hepatitis virus SH.

Eleven additional volunteers served as the test group to determine the effect of irradiation. Each was given 7 cc. of irradiated icterogenic serum by intramuscular injection. No untoward reaction was observed following inoculation.

12. Hanovia Chemical Manufacturing Co.

Postinoculation Follow-Up.—Tests of hepatic function were performed on all volunteers every seven to ten days for the first two months after inoculation and once to twice weekly thereafter. Examinations of urine for bilirubin and urobilinogen were performed on each volunteer two to four times weekly. The tests of hepatic function included the total serum bilirubin and one minute direct-reacting serum bilirubin, sulfobromophthalein sodium, cephalin cholesterol flocculation, serum colloidal gold and colloidal red flocculation, thymol turbidity and flocculation, urine bilirubin and urine urobilinogen tests. Visible scleral jaundice is usually present when total serum bilirubin values are greater than 1.4 mg. per hundred cubic centimeters.

RESULTS

The results are given in the table. Of 11 volunteers in the group of controls who received 4 cc. of nonirradiated icterogenic serum intramuscularly, in 2 hepatitis with jaundice developed after incubation periods of seventy-seven and eighty days. One volunteer had hepatitis without jaundice after an incubation period of eighty-seven days. Three volunteers after incubation periods of seventy-three to eighty days showed signs and symptoms compatible with the diagnosis of mild hepatitis without jaundice. The duration of symptoms and signs in these 3 was seven to twenty-one days. They exhibited malaise, lassitude, anorexia, nausea, occasional vomiting, discomfort in the right upper abdominal region and right upper quadrant tenderness, particularly noted in the right epigastrium. No significant change in the position of the liver edge was noted. At no other time during the period of observation were similar episodes encountered. None of these 3 volunteers had positive reactions to tests of hepatic function during or following their mild clinical illnesses. The observations did not suggest any other disease process. It was felt that, in view of the incubation period and the nature of the signs and symptoms, one would be justified in classifying the disease in these 3 cases as presumptive hepatitis. Similar observations have been made previously.[13]

Effect of Ultraviolet Rays on Hepatitis Virus SH

Group	Serum	Number Inoculated	Amount	Route	Results: No. With Hepatitis With Jaundice	Results: No. With Hepatitis Without Jaundice	Results: No. With Presumptive Hepatitis	Percentage With Hepatitis
Control.....	Virus SH, Fort Bragg strain	11	4 cc.	Intramuscular	2	1	3	47
	Mixture: virus SH, Fort Bragg strain and convalescent plasma	4	2 cc. serum; 10 cc. convalescent plasma	Intramuscular	1	0	0	
Ultraviolet ray test group	Virus SH, Fort Bragg strain	11	7 cc.	Intramuscular	0	0	0	0.0

Of 4 volunteers in the group of controls who had received a mixture of 2 cc. of nonirradiated icterogenic serum and 10 cc. of convalescent plasma, plus 20 cc. of convalescent plasma after 1, 2 and 3 months, in 1 hepatitis with jaundice developed after an incubation period of ninety-three days. None of the 4 volunteers who received 10 cc. of convalescent plasma alone and served as controls to the aforementioned group showed any evidence of hepatitis.

The incidence of hepatitis in the group of 15 controls, therefore, was 47 per cent, if one includes the 3 cases of presumptive hepatitis. If the 3 subjects with presumptive hepatitis are excluded, the incidence of 4

12. Neefe, J. R.; Stokes, J., Jr.; Garber, R. S., and Gellis, S. S.: Studies on the Relationship of the Hepatitis Virus to Persistent Symptoms, Disability, and Hepatic Disturbance ("Chronic Hepatitis Syndrome") Following Acute Infectious Hepatitis, J. Clin. Investigation 22:329 (March) 1943.

undoubted cases of hepatitis in 15 volunteers is 27 per cent. The maximum total serum bilirubin values in the 3 controls with jaundice were 7.9, 1.6 and 3.1 mg. per hundred cubic centimeters.

Of the group of 11 volunteers, each of whom received 7 cc. of irradiated serum intramuscularly, none showed the slightest clinical or laboratory evidence of hepatitis during an observation period of five months. It should be noted that the dosage used, 7 cc., was almost double that used for the controls.

It was deemed advisable to determine whether allergy had developed in the volunteers who received the irradiated serum as a result of any altered protein that might have been present. Preliminary electrophoretic and biochemical studies of plasma similarly exposed to ultraviolet rays had demonstrated no alterations in the plasma proteins except for slight reduction in prothrombin and complement. It was necessary, therefore, to determine by clinical trial whether or not subsequent injections of irradiated plasma might give rise to allergic manifestations, because of sensitization resulting from any minimal protein changes.

Irradiated normal plasma which had received the same exposure as the icterogenic serum was injected intradermally, intramuscularly and intravenously in amounts of 0.1 cc., 1.0 cc. and 10.0 cc., respectively, in a group of 5 volunteers who had originally received irradiated serum. In addition, the same tests were carried out on an equal number of controls. No allergic response or untoward reaction was noted following these tests. Five additional volunteers who had originally received the irradiated serum were then tested for sensitivity with larger injections of irradiated plasma. Each was given 10 cc. of irradiated plasma intravenously. No untoward response was observed during a forty-five minute period of observation. Each was then given an intravenous injection with amounts of irradiated plasma ranging from 75 to 150 cc. There was no immediate or delayed reaction, and their temperatures remained normal. Clinical sensitivity studies, therefore, seemed to substantiate the lack of important electrophoretic and biochemical alterations in the irradiated plasma.

COMMENT

The incidence of hepatitis in the groups of controls, including the 3 cases of presumptive hepatitis, was 47 per cent as compared to 0 per cent in the test group that received irradiated serum. Whether or not the 3 presumptive cases are included, these results are significant.

One of the principal factors involved in the amount of exposure that any given material receives in the apparatus for irradiation, previously described, is the rate of flow of that material through the apparatus. Hampil and her co-workers [14] have shown that neurotropic viruses in general, with the exception of rabies virus, are more resistant and require a slower rate of flow for inactivation than a number of other viruses. Since hepatitis virus SH has been shown to be unusually resistant to various physical and chemical agents, it was felt that the infective serum should be exposed to irradiation within the rate of flow range employed for inactivation of certain neurotropic viruses previously tested.

Another important factor was the possible alteration of serum proteins by irradiation. With the method employed, the earliest detectable protein changes are found with a rate of flow of 16 cc. per minute. The rate of flow in this study was 24 cc. per minute. Chemical fractionation and electrophoretic studies of normal human plasma irradiated at the same rate of flow as the icterogenic serum revealed no alteration of proteins except for a slight decrease in prothrombin and complement. In the relatively small number of cases studied, no allergic manifestations developed in members of the test group when later studied for acquired sensitivity by intradermal, intramuscular and intravenous injections of irradiated normal plasma.

Since there are no laboratory methods for the detection of virus SH in plasma and serum, it is apparent that inadvertent administration of icterogenic blood products cannot be avoided unless certain measures, such as carefully controlled routine exposure to ultraviolet rays of human plasma and serum, would render them safe for administration.

Oliphant [14] pointed out that the factors of titer of the icterogenic agent and the dose of serum given could possibly have an influence on the "icterogenic capacity" of irradiated material. Both in his experiments and in the present one, there was no possibility of determining the importance of these factors.

The preparation of virus vaccines by exposure to ultraviolet rays of suspensions of virus suggests the possibility of producing a vaccine for homologous serum hepatitis using known icterogenic materials. Whether or not hepatitis virus SH retains its antigenic properties following inactivation is not known. The resistance of the subjects inoculated with irradiated serum will be tested later. With no method of estimating the concentration of virus SH in a given amount of serum or plasma and no method of concentrating the virus, one might find it difficult to produce a reliable method for immunization.

SUMMARY AND CONCLUSIONS

A practical, safe and effective method for irradiating icterogenic serum and plasma is presented. Of 15 volunteers who received nonirradiated icterogenic serum, in 3 hepatitis with jaundice developed, in 1 hepatitis developed without jaundice and 3 had presumptive hepatitis. Of 11 volunteers who received irradiated icterogenic serum, none showed any evidence of hepatitis. Similarly irradiated plasma revealed no alteration of the electrophoretic pattern. By chemical fractionation methods, the plasma proteins were essentially normal. There was a slight decrease in prothrombin and complement. The initial inoculation of 11 volunteers with irradiated serum produced no untoward reaction. Subsequent inoculation of 10 of these volunteers with irradiated plasma intradermally, intramuscularly and intravenously, revealed no evidence of acquired sensitivity. This clearcut result strongly favors the routine use of exposure to ultraviolet rays of serum and plasma under properly standardized conditions.

14. Personal communication to the authors.

Cost of Radioactive Materials.—Use of the facilities and by-products of the reactor at Oak Ridge has increased tremendously the supply of radioactive materials, progressively reduced their costs to qualified research agencies, and brought many of the rarer substances within reach of the ordinary technician. A report issued by the United States Commission on the completion of the first year of the isotope program gave examples. One millicurie of carbon 14, if produced by using a cyclotron, would cost approximately $1,000,000; the same amount manufactured in the atomic piles of Oak Ridge is being sold at $50. —The Department of State publication 3161, General Foreign Policy Series 3, released June 1948.

INHALATION OF PENICILLIN DUST

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The preliminary results obtained with the inhalation of penicillin dust indicate that this is an effective and practical method in the treatment of many types of infections of the respiratory tract.[1] The present report is a more extensive study of this procedure carried out on 357 patients from October, 1946.[2] In this study more inclusive information has been obtained on the following aspects of the problem: the incidence and nature of allergic reactions occurring with the method, an evaluation of the efficiency of this method in a large number of patients, particularly those with bronchiectasis, and a further refinement of the method to increase its practicality for home, office and hospital use.

APPARATUS

The apparatus devised for this purpose delivers a fine nonirritating penicillin dust to the respiratory tract. It is simple mechanically and therefore lends itself to immediate use, when such treatment is indicated, in the hospital, office or home.

The original device consists of an oronasal face piece, which is held on the face by an elastic head band (fig. 1). The front of the mask contains a large exhalation valve (A) in direct line with the stream of exhaled air. The portion of the mask beneath the chin contains a rubber sleeve (C) fitted with an inhalation valve (B) which directs the inhaled air in a plane at right angles to the stream of exhaled air. The inhalation valve is fitted with a detachable metal chamber (D) containing the penicillin dust. The chamber is fitted with a fine rayon wire mesh platform (E), on which the penicillin dust is placed. During inhalation, the air is drawn through this platform and lifts the penicillin dust through the inhalation valve into the airways. The penicillin dust is protected against exhaled moisture by the one way inhalation valve and the arrangement by which the exhaled air is released in the plane at right angles to the inhaled air. There is a hole in the top of the mask about 6 mm. in diameter. This additional air inlet avoids any feeling of resistance on inspiration and is necessary in order to keep the amount of inhaled penicillin dust at optimum quantities. The penicillin dust used in this study was crystalline sodium penicillin G, processed to no. 50 to 100 mesh particles.[3]

Recently a modification of this apparatus was constructed (figs. 2, 3 and 4) to deliver penicillin dust more thoroughly throughout the respiratory tract.[4] This device consists of a molded plastic discharge chamber, a detachable mouth piece and an alternate molded nose piece. The penicillin dust is contained in a small plastic cartridge, the bottom of which is fitted with a fine mesh wire screen, through which the penicillin dust is released. The upper rim of the cartridge exhibits two small flanges, which fit into a groove and allow locking the cartridge in position in the discharge chamber. The distal end of the discharge chamber is formed into a curved tube runway containing an aluminum ball. On inhalation the aluminum ball is rapidly drawn up the runway until it strikes the cartridge containing the penicillin; the impact causes a release of a small amount of the penicillin dust into the discharge chamber. The upper end of the runway is grooved, so that the air to be inspired can by-pass the aluminum ball after it strikes the cartridge; the air to be inspired, as it by-passes the ball, carries the released penicillin dust directly into the respiratory passages. Thus, with each respiration a small but uniform amount of dust enters the respiratory passages until the total dose has been consumed; this is usually accomplished within three to five minutes. This is an advantage over the original device, which did not control the amount of dust per inhalation. Expiration is effected by breathing around the inhaler, through the nose if the mouth piece is used, through the mouth if the nose piece is used or by removing the inhaler from the mouth during expiration.

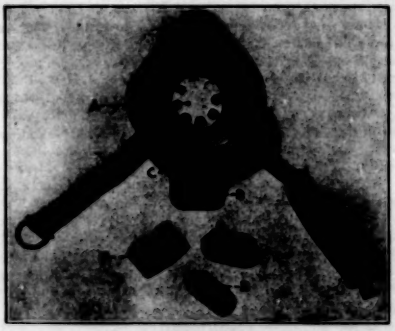

Fig. 1.—Oronasal mask for inhalation.

By omitting the valve mechanism for exhalation, it has been possible to reduce the loss of drug adhering to the apparatus surfaces to 10 per cent, as determined by assaying the penicillin content remaining in the inhaler after treatment is completed. This obviates one of the disadvantages of the mask used in the original work, as the mask has a larger surface to which penicillin may adhere.

PROCEDURE

Twenty normal subjects (including the authors) were used as an experimental group to determine any untoward effects of inhaling penicillin dust. This group was also used to establish penicillin blood level curves. Three hundred and fifty-seven patients with various types of infections of the upper and lower parts of the respiratory tract (table 1) were treated by this method; 174 were hospitalized and 183 were ambulatory. All hospitalized patients received 100,000 units of penicillin dust three times a day. Inhalations were continued until all the dust was inhaled, usually three to six minutes. Patients were instructed to refrain from eating or drinking for one hour following the treatment, to avoid washing down the penicillin dust from the

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1. Krasno, L.; Karp, M., and Rhoads, P. S.: Inhalation of Penicillin Dust, Science **106**: 249-250 (Sept. 12) 1947.

2. Since this paper was written there have been 160 additional cases, making a total of 517 patients treated with the inhalation of penicillin dust.

3. The penicillin for this study was processed by and furnished by the Abbott Laboratories, North Chicago, Ill.

4. This device for the inhalation of penicillin dust was originally developed by the Abbott Laboratories. The authors cooperated by offering suggestions for improvements on the original model.

posterior pharyngeal wall. The bronciectatic patients received 100,000 units of penicillin dust three times a day for seven to ten days in the hospital, and the same regimen was continued for another week at home. During the third week 100,000 units of penicillin dust were inhaled one to two times a day, depending on the

Fig. 2.—*A*, mouth inhaler disassembled. *B*, sagittal section of mouth inhaler assembled.

requirements. There was gradual reduction in the number of treatments per week until the optimum number of treatments per week needed for maintenance of comfort was determined. Ambulatory patients received 100,000 units of penicillin dust one to three times a day, depending on the particular condition involved. Ambulatory bronchiectatic patients received one daily treatment at the office and two treatments at home for ten days. Thereafter the regimen followed was similar to that of hospitalized patients. Throat and nose cultures prior to first treatment and after last inhalation were made for all hospitalized patients. In the first 68 patients treated with this method, daily nose and

Fig. 3.—Mouth inhaler assembled (without penicillin cartridge) (A) and molded detachable nose piece (B).

throat cultures were obtained. Bacteriologic examinations of sputum were done when specimens were obtainable. The clinical progress of the patient was followed by the report of the patient, his physician and the authors. The duration of treatment for each subject was determined bacteriologically and by the clinical progress made. Approximately two thirds of the subjects had less than three treatments. The highest number was reserved for the patients with chronic bronchitis, chronic sinusitis, bronchiectasis and bronchial asthma. It was not practical to obtain laboratory data for some of the ambulatory patients. However, this group gave added information regarding the clinical progress and allergic aspects of this type of treatment.

At the present time experiments are being conducted with streptomycin dust. One third of a gram of streptomycin and 100,000 units of penicillin are given three times a day. Experimental work is also being done on the distribution of the penicillin dust particles in the respiratory tract. The data obtained will be presented in a subsequent report.

RESULTS

The clinical conditions treated are tabulated in table 1. Two hundred and thirty-nine subjects (67 per cent) presented infections of the upper part of the respiratory tract, 169 of whom had symptoms of the "common cold." One hundred and ten patients (30 per cent) had infections of the lower part of the respiratory tract. Eight patients received penicillin dust as prophylaxis in the preoperative and postoperative management of surgical interventions.

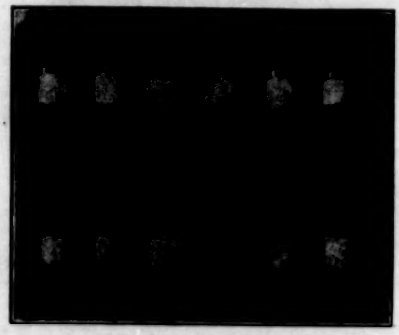

Fig. 4.—Cartridges boxed and ready for use. Each cartridge contains 100,000 units of penicillin.

TABLE 1.—*Clinical Diagnosis of 357 Patients Treated (174 Hospital Patients; 183 Outpatients)*

Clinical Diagnosis	Number of Cases
I. Infections of the Upper Part of the Respiratory Tract	
"Common cold" (acute rhinitis and/or nasopharyngitis)	169
Subacute and chronic nasopharyngitis	39
Acute and chronic sinusitis	30
Acute and chronic laryngotracheal bronchitis	6
II. Infections of the Lower Part of the Respiratory Tract	
Bronchiectasis	39
Acute and chronic bronchitis	41
Bronchial asthma with acute or chronic bronchitis	24
Pneumonia	6
Pulmonary abscess	1
III. Miscellaneous	
Preliminary treatment for operation	8
Prophylactic treatment following operation	3

Tables 2, 3 and 4 present bacteriologic data [5] obtained from throat, nose and sputum cultures prior to and following completion of the course of inhalation therapy.

5. These charts represent bacteriologic data based on the first 39 hospitalized patients treated. The bacteriologic results obtained in the remaining hospitalized patients were essentially the same.

There was a decided reduction in the number of, or complete disappearance of, gram-positive bacteria, as determined by bacterial cultures from the nose, throat and sputum. In many instances there was a decided decrease in the number of gram-negative bacteria that could be cultured from the same areas following the inhalation of penicillin dust. Not infrequently these results were accomplished following one inhalation treatment. Figure 5 illustrates a blood agar plate of a throat culture prior to the inhalation of 100,000 units of penicillin dust. The profuse growth of streptococcic colonies is entirely absent on plate B, which contains a culture of a specimen taken two hours following the inhalation of 100,000 units of penicillin dust. Another culture, made twenty-four hours after treatment, showed no growth of bacteria. Penicillinase was added to all cultures, so that any penicillin present in the material obtained for culture would be neutralized; thus, favorable changes in the bacterial flora of the upper part of the respiratory tract, as evidenced by the bacteriologic results reported in tables 2, 3 and 4, reflect the beneficial effects with the penicillin dust in situ and are not the results of penicillin being carried over into the culture medium and exhibiting a bacteriostatic effect in vitro.

Table 2 illustrates the effect of dry penicillin on the various types of organisms seen in the throat. The material in the table is arranged according to the extent of the growth of a given organism before and after the course of treatment. It is interesting to note that all of the organisms, including gram-negative bacteria, were appreciably influenced by the treatment. Prior to inhalation of penicillin dust 14 patients had a heavy growth of Streptococcus viridans, 10 showed a moderate growth and 1 had a light growth. After a course of treatment, there was 1 instance of heavy growth, 4 of moderate growth, 7 of slight growth and 13 of no growth after seventy-two hours of incubation on blood agar plates. In the cases of Diplococcus pneumoniae there was one of heavy growth, 10 with moderate growth before inhalation of dry penicillin. After treatment the Diplococcus pneumoniae disappeared in all 11 patients.

Table 3 indicates that organisms in the nose quickly disappeared after inhalation of dry penicillin.

Table 4 illustrates the effects of the treatment on the sputum specimens. Before treatment 6 patients showed a heavy growth of S. viridans and 5 a moderate growth. After inhalation of dry penicillin there was a slight growth in 4 cases and no growth in 7 cases. In 1 case there was a moderate growth of D. pneumoniae and a slight growth in 2, which disappeared in each instance following treatment. In 2 cases there was a moderate growth of Streptococcus hemolyticus, which completely disappeared after inhalation.

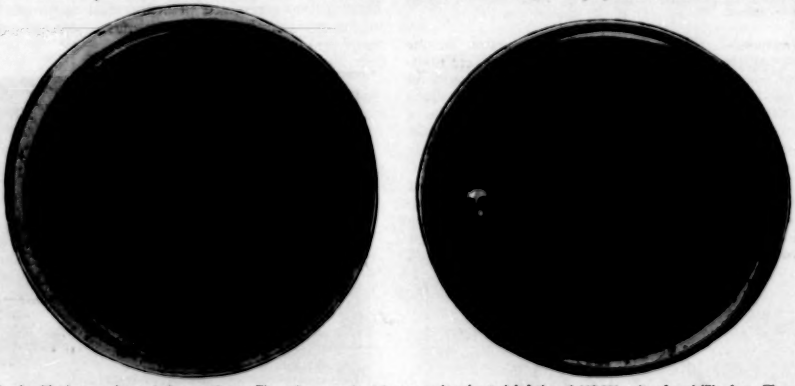

Fig. 5.—Blood agar plates of throat culture. The culture on the left was made prior to inhalation of 100,000 units of penicillin dust. The culture on the right was made two hours following the inhalation of 100,000 units of penicillin dust (penicillinase was added).

TABLE 2.—*Summary of Bacteriologic Data from Throat Cultures*

Organism	Growth Before Treatment			Growth After Treatment			
	Heavy	Moderate	Slight	Heavy	Moderate	Slight	No Growth
α hemolyticus streptococci (Str. viridans)	17*	13	1	1	4	9	16
β hemolyticus streptococci (Str. hemolyticus)	2	1	..	..	..	..	3
Diplococcus pneumococci	1	10	..	..	..	..	11
γ anhemolyticus streptococci	..	4	..	..	2	..	2
Staphylococcus aureus	1	10	3	..	7	3	4
Staphylococcus hemolyticus aureus	1	4	..	..	..	..	5
Staphylococcus albus	5	17	2	..	10	4	10
Neisseria catarrhalis	..	11	2	..	6	4	3
Micrococcus tetragenous	..	3	..	..	..	..	3
Aerobacter aerogenes	..	1	..	..	..	1	0
Bacillus hoffmanni	..	3	..	..	..	1	2
Diphtheroids	..	2	..	..	..	1	1

* Numerical values represent number of cases.

PENICILLIN BLOOD LEVEL CURVES

Figure 6 demonstrates blood levels observed when penicillin was inhaled by means of a mouth inhaler. Six subjects were given 100,000 units of penicillin and hourly blood levels were determined. The same 6 subjects were given 100,000 units of penicillin intramuscularly and comparable blood level determinations were made. The results demonstrate that the peak level is reached in one hour and that therapeutic levels are sustained for about a five hour period.

ALLERGIC REACTIONS

In the first 160 patients treated with the mask the incidence of allergic reactions was 6 per cent. With one exception these reactions were local in character and were manifested as contact dermatitis, stomatitis and posterior pharyngeal irritation. One case was

noted of generalized maculo-papular eruption and itching without other systemic manifestation. Creaming the face with wool fat before and washing with bland soap and water following treatment helped to minimize the reaction considerably in the patients in whom contact dermatitis developed. Since this protective regimen was instituted the incidence of contact dermatitis has been reduced to 3 per cent in a subsequent group of 197 patients.

The nature and extent of allergic reactions noted with the inhalation of penicillin dust have been altered since the plastic mouth inhaler has been put into use. There has been, so far, no evidence of contact dermatitis noted with the use of the mouth inhaler. There is little chance of penicillin dust coming in direct contact with the skin of the face. The reactions noted with the mouth inhaler have been primarily those of posterior pharyngeal irritation and stomatitis. Up to the time of writing, 3 per cent of the patients exhibited this type of reaction with this device. There were no instances of angioneurotic edema of the upper respiratory passages or generalized anaphylactoid manifestations with the use of the mask or the mouth inhaler in over 357 cases.

The development of contact dermatitis is no contraindication to continuing treatment, provided that the

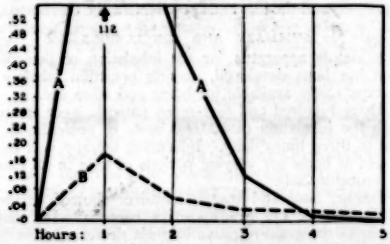

Fig. 6.—Average blood levels of penicillin obtained in 6 subjects. *A* indicates blood levels following 100,000 units of penicillin given intramuscularly, and *B*, blood levels following the inhalation of 100,000 units of penicillin dust. The vertical column shows units of penicillin per cubic centimeter of serum.

patient is seriously in need of such treatment and precautions are taken to protect the patient locally and with antihistaminic drugs. Continued use in patients in whom contact dermatitis develops has, as yet, failed to produce any untoward systemic reactions.

GENERAL RESULTS

The clinical results from the inhalation of penicillin dust have been gratifying (table 5). Some conditions responded dramatically, while others progressed slowly, requiring more persistent treatment. In most instances, however, it was believed that this form of treatment was of definite value. The bronchiectatic patients serve, perhaps, best for evaluation of clinical results. In these patients spontaneous remission of the disease is not likely to occur. The results obtained in these patients in our series can be attributed justifiably to this particular type of treatment. In this group improvement of varying degree was obtained in all cases.

The patients with bronchial asthma and chronic bronchitis had moderate to decided improvement, the infectious condition almost disappearing, although the allergy persisted to a decreased degree. Patients with asthmatic conditions of bacterial origin improved remarkably.

The patients with acute rhinitis and laryngotracheal bronchitis usually recovered completely within one to three days. The "common cold" syndrome of acute rhinitis, lacrimation, nasopharyngitis and general malaise responded to inhalation therapy. Forty-two per cent were considered cured; 38 per cent were judged as 3 plus improved. In many instances the penicillin dust seemed to exert a vasoconstrictor action

TABLE 3.—*Summary of Bacteriologic Data from Nose Cultures*

Organism	Growth Before Treatment: Heavy	Moderate	Slight	Growth After Treatment: Heavy	Moderate	Slight	No Growth
α hemolyticus streptococci	..	2*	..	..	..	..	2
β hemolyticus streptococci	1	1	..	..	..	..	2
Diplococcus pneumococci	..	..	..	..	..	..	1
γ anhemolyticus streptococci	..	1	..	..	..	..	1
Staphylococcus aureus	..	2	..	..	..	..	2
Staphylococcus aureus hemolyticus	..	2	..	..	..	1	..
Staphylococcus albus	..	7	4	..	1	2	5
Neisseria catarrhalis	..	1	1	..	..	..	2
Bacillus proteus vulgaris	..	1	..	..	..	..	1

* Numerical values represent number of cases.

of the mucous membrane of the nose and throat. Patients stated that they could breathe more freely through the nose and the stuffiness and congestion of the acute rhinitis often improved immediately after treatment. Also, on occasion the pain of an acutely sore throat was ameliorated in one-half to one hour following a treatment. These phenomena cannot be fully explained on the basis of the known properties of penicillin and need further investigation.

BRONCHIECTASIS

The aerosol method probably has its greatest merit in diseases affecting the surfaces of the bronchi, such as in bronchitis and bronchiectasis. The most notable results were obtained in bronchiectatic patients who showed toxic absorption from the disease process, as evidenced by loss of weight, low grade fever and profuse amounts of sputum. Pathologic changes were evident on roentgenologic examination. Thirty-eight patients with bronchiectasis were treated. Thirty of the patients received inhalation of 100,000 units of penicillin

TABLE 4.—*Summary of Bacteriologic Data from Sputum Cultures*

Organism	Growth Before Treatment: Heavy	Moderate	Slight	Growth After Treatment: Heavy	Moderate	Slight	No Growth
α hemolyticus streptococci (Str. viridans)	6*	5	..	..	..	4	7
β hemolyticus streptococci	..	2	..	..	..	..	2
Diplococcus pneumococci	..	1	2	..	..	..	3
γ anhemolyticus streptococci	..	2	..	..	1	..	1
Staphylococcus aureus	3	3	..	..	2	2	2
Staphylococcus albus	1	6	..	..	5	..	1
Neisseria catarrhalis	..	3	1	..	2	2	..
Micrococcus tetragenous	..	1	..	..	..	..	1
Bacillus mucosus capsulatus	..	2	..	..	..	..	2
Neisseria pharyngis sicca	..	..	1	..	..	..	1

* Numerical values represent number of cases.

dust three times daily for varying periods of time. Eight received combined parenteral and inhalation therapy.

Twelve of the 38 patients (32 per cent) with bronchiectasis showed much improvement, as evaluated by the patients, attending physicians and authors. The disease in these patients had remained in a quiescent form two to eight months following the course of

treatment, with one to two inhalations of penicillin dust a week to maintain them free from infections of the respiratory tract.

One patient had a large pulmonary abscess complicating his bronchiectasis. This cleared up gradually following two hundred and ten inhalations of penicillin dust during his hospital stay and ninety similar treatments at home. Seventeen patients (44 per cent) were considered moderately improved. Three were given a series of treatments before and after lobectomy. The rest had only slight amelioration of symptoms.

Before the use of the present method, many patients with chronic pulmonary disease were not given adequate treatment because of the expense of prolonged hospitalization and equipment. The mask or inhaler utilizing dust aerosol permits the start of treatment in the hospital and continuation at home, or it permits a patient to go about his business without loss of time and with minimum expense.

Sufficient data are not available from our studies employing streptomycin dust to permit a clinical evaluation. Five patients have received this treatment for periods over ten days. The gram-negative bacteria have disappeared from the sputum in all instances, leaving a mild to moderate growth of yeast cells. In only 1 case stomatitis developed after three days of treatment. This cleared up in three days after use of the drug was discontinued.

TABLE 5.—*Results in 357 Patients Treated*

Clinical Diagnosis	Clinical Results *				
	0	+	++	+++	++++
I. Infections of the Upper Part of the Respiratory Tract					
"Common cold" (acute rhinitis and/or nasopharyngitis)	31	5	25	65	71
Subacute and chronic nasopharyngitis	..	2	7	9	5
Acute and chronic sinusitis	2	1	6	16	13
Acute and chronic laryngotracheal bronchitis	1	..	1	..	4
II. Infections of the Lower Part of the Respiratory Tract					
Bronchiectasis	..	..	6	17	121
Acute and chronic bronchitis	3	2	7	12	17
Bronchial asthma with acute or chronic bronchitis	2	2	7	9	4
Pneumonia	..	1	..	1	4
Pulmonary abscess	..	..	..	..	1
III. Miscellaneous					
Preoperative treatment	No result could be noted				
Postoperative treatment	No result could be noted				

* Clinical results expressed as 1, 2, 3 or 4 plus improvement.
† Numerical values represent number of cases.
‡ The patients with reactions of 4 plus had remained essentially symptom free to the time of writing.

COMMENT

One could anticipate the destruction of penicillin-sensitive organisms when placing penicillin dust at the bacterial site. There were, however, two unknown and important questions which could not be evaluated beforehand. First, would the inhalation of penicillin dust in 100 per cent concentration give rise to serious untoward reactions? Second, what clinical results would be obtained by such a procedure? Among 357 patients treated by inhalation of penicillin dust the allergic reactions were less than would have been anticipated. The best explanation is that penicillin in dust form (50 to 100 mesh in size) is absorbed over a relatively long period of time. Slow absorption is indicated by the presence of therapeutic blood levels four to five hours after inhalation. The rate and extent of absorption of an antigenic substance modifies the nature of the response to that substance. It is theoretically possible that the desensitization of penicillin-sensitive persons may be taking place by virtue of a slow absorption phenomenon. In view of the paucity of systemic reactions it appeared justifiable to continue to treat seriously ill patients, such as those with bronchiectasis, in spite of the presence of contact dermatitis. Continuation of such procedure has not as yet produced any systemic reactions. In 1 case the contact dermatitis eventually disappeared and did not recur with subsequent treatment.

The authors are aware of the difficulties attendant on the evaluation of clinical data. However, the clinical results obtained from this dry aerosol therapy were most gratifying. The method is simple and inexpensive. One hundred and thirty-four patients (37.5 per cent of all patients treated) were judged as greatly improved and 129 patients (36 per cent) as moderately improved. Therefore, 73.5 per cent of the entire group had a satisfactory amelioration of symptoms.

It should be emphasized that only in relatively mild bacterial infections of the upper respiratory passages can penicillin dust be relied on as the total treatment, and, if there is not a rapid response in these cases, parenteral antibiotic administration, biologic therapy or treatment with sulfonamide drugs may be necessary. In such diseases as chronic sinusitis, bronchiectasis and bronchial asthma associated with infection, measures directed at securing drainage, combating allergies, liquifying and the like must supplement the treatment.

SUMMARY AND CONCLUSIONS

A simple apparatus for the inhalation of penicillin dust has been developed, making penicillin inhalation therapy easily available for home and office use.

Three hundred and fifty-seven patients were treated with the inhalation of 100,000 units of penicillin dust one to three times daily. Inhalation therapy was continued at home for varying periods of time in all cases of bronchiectasis.

Throat, nose and sputum cultures showed decided diminution of the gram-positive bacteria. In many instances the gram-negative bacteria decreased also.

Penicillin blood level curves indicated absorption from the respiratory tract. Maximum levels of penicillin in the blood are obtained one hour after inhalation. Therapeutic levels are maintained for a period of five hours following the inhalation.

The incidence of allergic reaction in the 357 patients treated by this method was 3 to 6 per cent. The reactions were local in character, manifested as contact dermatitis, stomatitis and posterior pharyngeal irritation. It would seem that the gradual rate and extent of absorption of penicillin dust may account for the low incidence of systemic reactions.

The continued use of penicillin dust in seriously ill patients (with bronchiectasis) in whom contact dermatitis develops failed to produce any systemic reactions.

This method lends itself particularly to the treatment of bronchiectasis. Initial improvement can be obtained usually within ten days to two weeks and can be maintained by continued treatment at home.

Streptomycin dust is now being used, and with the exception of 1 case of stomatitis no untoward reactions have been noted.

While inhalation of penicillin dust almost invariably produced improvement in all types of bacterial infections of the upper part of the respiratory tract, it should again be emphasized that it cannot always be relied on as the total treatment of these infections, to the exclusion of intramuscular or intravenous administration of penicillin, attention to allergic sensitivity, local drainage of sinuses and bronchiectatic cavities and the like.

V 13
1948

GENERAL PRACTITIONERS SESSION

THE UNKNOWN DIABETIC AND HOW TO RECOGNIZE HIM

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The diagnosis of diabetes mellitus, in a frank instance of the disease, is one of the easiest that can be made reliably. Even in patients who are symptomless, diagnosis is possible on the basis of a dependable determination of the level of sugar in blood taken from the patient after twelve or fourteen hours of abstinence from food. With the Folin and Wu technic for blood sugar analysis, the finding of something more than 120 mg. per hundred cubic centimeters of reducing substance expressed as dextrose establishes the fact of diabetes with an error which is smaller, I suspect, than that involved in the diagnosis of any other disease. A degree of overstatement is involved in this assertion and certain reservations will be mentioned later.

On the other hand, to be able to affirm with confidence that glycosuria in a given person is significant of diabetes when the fasting blood sugar is lower than 120 mg. per hundred cubic centimeters requires much discrimination. In cases such as this difficulties are encountered and a considerable incidence of error is involved. Mistakes are made in both directions. On the one hand, mild but potentially disabling diabetes is not infrequently neglected, and on the other hand persons are labeled diabetic on insufficient evidence. I could cite numerous examples of patients who, on one examination, showed a trace of sugar in the urine which was ignored at the time by their physicians and who later returned with frank diabetes mellitus. In many of them the fasting blood sugar was determined and a normal value was obtained. I also could cite instances in which significant injustice has resulted because a diagnosis of diabetes mellitus was based on an improperly interpreted dextrose tolerance test, with the result that the person either was denied life insurance or had to pay an increased premium for insurance. Which of the two mistakes is considered the more serious depends on points of view. Both are regrettable, but if I had to choose between them I should say that the advantage to persons with potential diabetes of being put on their guard and thereby protected against development of frank disease outweighs the occasional injury to persons for whom a diagnosis of diabetes is unjustified. In other words, I prefer to err, if err I must, on the side of certainty that there is no diabetes. A good rule, in my opinion, is to regard all positive reactions for reducing substances in the urine as indicative of diabetes mellitus until proved otherwise, but to obtain in all such cases an examination of the blood and, if this is normal, an oral dextrose tolerance test. If the result of the tolerance test is surely negative all is well and good; if it is distinctly positive, even when the fasting blood sugar level is normal, the disease is diabetes mellitus; if the test is equivocal, which unfortunately is not infrequent, a diagnosis is unjustified but reexamination later or repeatedly ought to be carried out.

From the Division of Medicine, Mayo Clinic.

Read in a panel discussion on Treatment of the Ambulatory and Hospitalized Diabetic Patient at the interim meeting of the American Medical Association, Cleveland, Jan. 8, 1948.

MELITURIA ALONE NOT DIAGNOSTIC

All too often diabetes has been diagnosed on the sole basis of a finding of some reducing substance in the urine. This is inexcusable, since a number of benign conditions are thereby mistakenly labeled diabetes mellitus. Such patients are subjected to the injury of whatever stigma attaches to the diagnosis of diabetes; they also not infrequently are subjected to unnecessary restrictions of their diets or, worse still, to injections of unneeded insulin. The possibility of error in diagnosing diabetes from urinary tests alone is very great. The incidence of nondiabetic melituria is high. In a series of insurance examinations reviewed by Exton[1] diabetes was responsible for positive results of urinary tests in only about half of 800 specimens of urine in which the amount of reducing substance expressed as dextrose was 1 per cent or less. The positive results in the balance of the specimens were caused by something other than dextrose or, if due to dextrose, diabetes could be ruled out by a tolerance test. If the reducing power of the urine is more intense, with the reducing substance, expressed as dextrose, exceeding 1 per cent, the likelihood of error is diminished. In 97 per cent of 200 such specimens of urine the reducing substance was dextrose. However, in some of them blood sugar levels remained within normal range on an oral tolerance test so that diabetes mellitus could be excluded.

Reducing substances other than dextrose which appear in the urine include lactose, galactose, fructose, maltose, mannoheptulose and pentose. It also has been suspected that ascorbic acid (vitamin C) may, at times, provoke positive urinary tests. This, however, seems unlikely, since the reducing power of ascorbic acid is something less than that of dextrose, and even very large therapeutic doses (1,000 mg.) seem not to be sufficient to affect the reducing power of the urine. Specific chemical tests are available for the identification of the sugars other than dextrose found in urine, but such identification represents a refinement of little practical importance. None of these other meliturias affect the patient's health, and the amount of any of these substances in the blood probably never is sufficient to influence significantly the reducing power of the blood, whereas the diagnosis of diabetes depends primarily on the level of sugar in the blood.

BLOOD SUGAR VALUES

I stated earlier that a fasting venous blood sugar value of 120 mg. or more per hundred cubic centimeters is acceptable, with certain reservations, as diagnostic of diabetes mellitus. Infections, recent injuries or hyperthyroidism may elevate the concentration of blood sugar and confuse the issue; so also may hyperpituitarism, functioning adrenal tumors, encephalopathies and acute coronary occlusion. Occasionally the blood sugar level rises in renal failure and likewise with arteriosclerotic changes of the kidneys. Due allowance must be made for such conditions. Fasting blood sugar values tend to rise with age. However, they seldom normally exceed 120 mg. per hundred cubic centimeters. On the other hand, low fast-

1. Exton, W. G.: Differential Diagnosis of Conditions Associated with Sugar Excretion, New York State J. Med. 36:1545-1553 (Oct. 15) 1936.

ing values for blood sugar occur in true diabetes mellitus, and care must be taken not to be misled by them. In many cases, especially in children, a stormy onset of diabetes is followed by remission which may last for several months, and in this period fasting blood sugar values may fall within the normal range. Likewise in many cases of mild diabetes restriction of the diet is sufficient to bring fasting values down to normal levels. Malingerers effect the same either by fasting or by taking a dose of insulin shortly before the time of examination. In such instances, examination of the urine and blood for sugar forty-five to sixty minutes after a meal liberal in carbohydrate may be helpful, especially if the value then is found to be not less than 180 mg. per hundred cubic centimeters. Otherwise a tolerance test is indicated.

THE DEXTROSE TOLERANCE TEST

The dextrose tolerance test should not be made if the diagnosis of diabetes has previously been established either from the history or from the finding of an abnormal elevation of the fasting blood sugar. It gives imperfect information about the severity of diabetes, and the ingestion of the necessary amount of dextrose is not without injurious potentiality when the diabetes is of much severity.

There is no unanimity of opinion as to how the tolerance test should be conducted. Consensus favors the one dose, three hour test with a solution of dextrose administered by mouth and determinations of blood and urinary sugar made before and at spaced intervals after the patient begins to drink the solution. Whether 50 or 150 Gm. of dextrose is given makes little difference. The dose commonly employed is not less than 50 nor more than 100 Gm. for adults and 1 Gm. for each pound (0.5 Kg.) of body weight for children. Authorities agree that the patient should have fasted during the twelve or fourteen hours before the test is made, and that his diet must not have been restricted for at least three days beforehand. The majority of those experienced with the test place little emphasis on the peak of the blood sugar elevation that follows the ingestion of the dextrose in thirty to sixty minutes. They regard as more important diagnostically the rate of return of the blood sugar level to the normal range of fasting values (70 to 120 mg. per hundred cubic centimeters). The peak when the tolerance is normal rarely exceeds 180 mg. and rarely is accompanied by glycosuria. The return of the blood sugar level to the normal range of fasting values occurs between the second and the third hour. The peak in diabetes is attained later than the hour period and the return is retarded. Glycosuria accompanies the elevated blood sugar values.

Abnormal Responses; Not Diabetes.—Even a high peak which is accompanied by excretion of sugar in the urine is not considered diagnostic of diabetes mellitus when the blood sugar level returns to the range of normal fasting values within two hours. A response of this type is occasionally observed in hyperthyroidism; it also may be seen in patients who have undergone gastrectomy. It has been called the lag or storage type of response, but probably is explained on the basis of an increased rate of absorption of the dextrose.

A response of the sugar level of the blood which is normal in its pattern but is accompanied by glycosuria is interpreted as renal glycosuria. This is a benign condition dependent on a lowered glucose threshold in the kidneys. The amount of sugar in the urine will vary with the diet. It also varies from case to case with the degree of depression of the threshold. A threshold lower than the level of blood sugar during fasting permits continuous glycosuria. One higher than the fasting level but lower than the normal threshold is accompanied by discontinuous or cyclic glycosuria, the sugar appearing only after food is taken.

The renal threshold is depressed in pregnancy. This indeed is the explanation of most instances of the so-called melituria of pregnancy. The sugar excreted is dextrose, not lactose, as is frequently supposed. Lactosuria occurs uncommonly until lactation has begun.

The renal threshold usually is normal in diabetes mellitus but occasionally may be depressed. Sugar then will be excreted even when the treatment of the diabetes with diet or insulin or both is adequate in all respects. The diabetes in patients with this abnormality is difficult to treat, for the reason that tests of the urine of these patients serve imperfectly as guides to the desirable dosages of insulin.

Pseudodiabetic Responses.—The same conditions which may elevate the fasting level of the blood sugar of normal persons modify the response of the blood sugar level in the glucose tolerance test. They include acute or chronic sepsis, physical injury, other endocrine diseases, especially hyperthyroidism, hyperpituitarism or active adrenocortical tumors, coronary occlusions, diseases of the liver, some encephalopathies, advanced chronic nephritis and muscular dystrophies. Furthermore, if a diabetic type of response is to be interpreted correctly the patient must not recently have engaged in unusual physical exertion or have taken alcohol or any drug, nor must he have been subjected to starvation, to a diet restricted in carbohydrate or to any recent emotional excitement. Tobacco smoking or chewing immediately before or during the test period will elevate blood sugar values, and apprehension over the venipunctures required by the test may provoke a diabetic type of response in some adults, but especially in young children.

In other words, tests for dextrose tolerance, if they are to give reliable results, must be made only under strictly basal (standard) conditions, and when any disease is present other than the suspected diabetes a positive response must be interpreted with caution. In the presence of another disease a diagnosis based exclusively on the results of a dextrose tolerance test can be no more positive than "diabetes suspected," but in that case other examinations should be made later and the patient should remain under the supervision of his physician until the suspicion is removed. True diabetes persists, so that in time a decision almost always can be reached, either on the basis of subsequent tests or as a result of the development of conspicuous symptoms. A diabetic-like response to the tolerance test is conclusive evidence of the presence of diabetes only in the absence of any other cause for disturbed carbohydrate metabolism.

DIABETIC SURVEYS

It is not to be doubted that many incipient cases of diabetes long remain unrecognized. Therefore knowledge as to the incidence of this disease can only

be obtained by satisfactory surveys and examination of all persons not previously diagnosed as diabetic. For such examinations some type of screening is required which involves a minimum of time and inconvenience for the persons examined. It might be wise to meet this problem by adopting a suggestion based on the opinion of many experts; namely, that if only one blood sample is available no other single determination of blood sugar is as useful as the one obtained two hours after the oral administration of a standard dose of dextrose. The briefest possible history also would be necessary because interpretation of a borderline two hour blood sugar value should properly be more severe when the person has a history of diabetes in his family.

The suggestion then would be to instruct examinees to eat freely of carbohydrate for three days and present themselves before the morning meal for testing, to give 50 Gm. of dextrose previously dissolved in 250 cc. of water flavored with citric acid and chilled and to secure after two hours a sample of arterial—that is, capillary—blood from finger or ear.

While there is advantage in use of venous blood in the type of dextrose tolerance test described before, British clinicians long have made their tolerance tests by using arterial blood. This is preferable in survey work, especially since micromethods are available so that a single drop of blood suffices for a satisfactory determination of sugar. The peak of the blood sugar response is higher when arterial blood is used than it is when venous blood is employed, but for the purposes of a survey we are not concerned with peak values and at two hours the differences between the sugar level in arterial and venous blood has disappeared. Therefore a value of 120 mg. or less could be taken as excluding diabetes, and one above that value would mean that the patient is a diabetic suspect. The procedure would, I think, pick out nearly all the persons having diabetes, although with them would be included a small group who did not have it. However, the positive but doubtful reactors could be subjected to more careful study afterward. For them I would resort to subsequent repeated observations until a diagnosis could be definitely established.

Less reliable for screening purposes would be a blood sugar determination obtained an hour after the morning meal, with this meal made rich in sweets and other carbohydrates. A blood sugar value of 170 mg. per hundred cubic centimeters would then represent the dividing point between persons who do not have diabetes and diabetic suspects.

Least reliable would be dependence on examination of the urine, although initial screening might be accomplished by testing urine collected after a breakfast which was rich in sweets and other carbohydrates. This would miss some diabetic persons, that is, those who had been on restricted diets earlier, but a brief history might suffice to pick up most of them. It would, of course, include many persons who were not truly diabetic, especially those with renal glycosuria. However, if the criterion adopted was a urine with not less than 1 per cent of reducing substance expressed as dextrose, most instances of melituria from sugars other than dextrose would be excluded.

The importance of early detection of diabetes cannot be overemphasized. Treatment now is usually postponed beyond the time when much restoration of pancreatic island function can be expected. Intensive management of diabetes offers greatest promise when it can be instituted at the very onset of the disease. However, this involves detecting the disease in its incipience, which rarely has been possible. For this reason all health examinations should include some screening tests for diabetes with a careful follow-up of the diabetic suspects which they disclose. An examination such as this made every year in all schools, college and other institutions, also in all business firms and factories, would contribute greatly to the public health. For this reason also the present active interest of the United States Public Health Service in undertaking diabetic surveys of communities, as in Oxford, Mass., and in Florida, should receive all possible support from practitioners of medicine and specialists in diabetes.

SUMMARY

The diagnosis of diabetes has been discussed with special reference to the significance of positive reactions for sugar in the urine, elevated blood sugar values and the oral dextrose tolerance test. The tolerance test can lead to error unless pseudodiabetic responses are recognized for what they are and the test is made under strictly basal (standard) conditions. Procedure for discovering, by survey, previously unrecognized diabetes also has been considered.

MEDICAL AND SURGICAL VASCULAR COMPLICATIONS OF DIABETES

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The term complication as employed in reference to a chronic disease is commonly used to refer to an associated disease as well as to a condition more directly the result, per se, of the primary condition.

In diabetes, a vascular complication, or associated vascular disease, is considered, as to degree at least, to be the direct result of the disturbed metabolic state, or greatly aggravated by it in both tempo and time.

Many pathologic conditions observed in the diabetic person are most favorably influenced through our ability to control the diabetes. Thus, for example, the person with controlled diabetes is less susceptible to infection and acidosis than the one with uncontrolled diabetes. Surgical procedures, acute and elective, trauma, neoplastic disease and even pregnancy—this latter if especially approached—do not present to the surgeon and internist a more formidable problem in the diabetic person than in the nondiabetic.

Premature vascular disease, with its interference with adequate circulation, does not seem to be so directly influenced in a favorable direction by good diabetic control alone. Since not all persons with diabetes over a period of years of diabetes contract premature and serious vascular damage, and since some persons with well controlled diabetes do contract early and serious vascular disease, perhaps one is justified in the following reasoning. Either some persons with diabetes are predestined to early vascular disease through heredity, and diabetes only aggravates this predisposition, or

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there is associated in a varying degree with diabetes, and more frequently with poorly controlled diabetes, a disturbance of fat metabolism which is in itself responsible for the vascular damage. At present our knowledge of the disturbed metabolism of diabetes is so limited, although it is currently rapidly increasing, that much of such reasoning is necessarily without basis of fact.

The major part of our attention to vascular disease in the diabetic person must be given to prevention. Limited by our present knowledge, we are confined as follows in this respect.

Many statistics show that vascular disease has a distinctly lower incidence in the presence of well controlled diabetes. Statistics to the contrary usually err because they are based on deficient records or too short periods of observation. Many of us have in our files case records of diabetes of twenty to twenty-five years' duration and over, in which it is impossible even by the most detailed study to demonstrate any evidence of vascular disease. There is, however, considerable evidence to indicate that fat should not be employed in the diet beyond that amount needed to supply adequate calories while prescribing liberal but subnormal amounts of carbohydrates. Also there is considerable evidence to support the theory that fats low in cholesterol are safest. As to protein, there is considerable evidence to justify the opinion that protein may be allowed without disadvantage, and frequently with distinct advantage, more liberally than has been done by many authorities in the past.

Improved effort to prevent or delay vascular damage in the future must follow amplification of our present knowledge of the disturbed metabolism.

Once vascular disease has developed to a degree that interferes with normal function, the problem in the person with diabetes, except for the necessity for control of the diabetes, is rather similar to that in the nondiabetic person.

In the diabetic patient vascular disease is most apt to be cardiovascular renal disease. Myocardial infarction, secondary to disease of the coronary arteries, is the major cause of death among persons with diabetes. Cerebrovascular accidents and vascular renal disease vie for second place. In the juvenile group renal disease is pressing for first place in the list of causes of death. Here we see most often the characteristic lesion of intercapillary glomerular sclerosis.

Gangrene of the lower extremities is a most frequent complication not uncommonly resulting in crippling amputation. Although it may occur in the absence of severe vascular damage, it is the degree of vascular damage that most frequently determines the susceptibility to, and the course of, infection and trauma in this area. Therefore great emphasis must continuously be placed on care of the feet, thus preventing as far as possible this serious complication. The greater the degree of vascular damage, the greater is the need for painstaking preventive effort and for adequate attention to minor lesions.

Hypertension is so commonly found associated with diabetes that the finding is almost expected past middle life. Among young persons with diabetes of over twenty years' duration, a national authority recently found hypertension present in 40 per cent. The hypertension associated with diabetes, in many instances at least, may or may not be the type of hypertension commonly classified as essential. The distinctly high incidence, however, is not denied.

Retinitis is probably the most discouraging vascular complication. Perhaps this is so discouraging because the incidence is so high among young persons. Dr. Priscilla White has recently found that 85 per cent of young persons with diabetes of over twenty years' duration showed evidence of retinitis. Other studies have indicated that the incidence is even more nearly universal than this figure. Although the incidence is distinctly lower among persons with continuously well controlled diabetes, there is an undeniable relationship between retinitis and duration of the diabetes. Early retinal damage may be slowed or even checked in its progress by the institution or reinstitution of exacting diabetic control. At present however, all other measures have proved to be of no assistance. However, reports of recent observations of the effects of rutin and hesperidine are promising in a somewhat limited percentage of the groups studied.

Vascular complications in the diabetic person are most often medical. The surgeon is relatively infrequently called on to assist, except when the lesion exists in a lower extremity or the eye. Antibiotics and the newer bactericidal drugs, especially the sulfonamide group, have proved a boon to the diabetic person. They have made it possible to bring infections under control quickly. They have lowered the mortality of elective surgical procedures. In the presence of vascular disease they have made it possible to carry out more conservative surgical procedures on the extremities than would have been attempted previously. For example, transmetatarsal amputation has not infrequently been successful in recent years with their assistance, whereas formerly only higher amputation would have been attempted.

Except for proper control of the diabetes, medical measures are largely directed at symptomatic relief, or at best are only retarding in their influence. Vascular antispasmodics of all types may be distinctly so classified. Spasm is not the controlling factor in vascular disease as it is seen in the diabetic person. For this same reason drugs or surgical procedures which produce sympathetic block at various levels produce only temporary relief.

Vascular disease among that group of diabetic persons with onset in childhood is especially disturbing because twenty to twenty-five years ago, shortly after the advent of insulin, our highest hopes for prevention of vascular disease rested in this group. The Joslin group has recently pointed out, however, that our current statistics in this regard are probably the worst that we will ever see, since these records being studied are those of diabetic persons who for not more than half of their diabetic life have had the advantage of good diabetic control.

At present there is a definite relationship between the incidence and degree of vascular disease in the person with diabetes, and the duration of the disease. At least until we know more of the facts regarding the total metabolic disturbance in diabetes, we must place our greatest confidence in our ability to maintain normoglycemia and aglycosuria in the presence of an adequate nutritional intake. We must diligently apply in a practical manner what knowledge we have today, for even tomorrow further light of great degree may be thrown on our problem. Let us not, either as physicians through failure to apply present accepted

therapeutic principles, or as patients through failure to give full cooperation, fail to maintain a physical status which will permit the patient to take advantage of the newer knowledge of tomorrow. As biochemists and physiologists slowly but progressively unfold further and further the manifold mysteries of metabolism, we will come to understand more thoroughly the problem of diabetes and be able to base on this knowledge a more effective therapy.

INSULIN AND DIET

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My colleagues and I, in common with all others dealing with diabetes, have long been disturbed by the increasing incidence of severe degenerative lesions in our patients. It appeared to us that data obtainable thus far from human beings were unsatisfactory as an aid in solving this problem, because of the impossibility of keeping such patients under sufficiently controlled conditions for sufficiently long periods of time. It seemed a reasonable expectation that if we could collect a series of diabetic animals and maintain them with known amounts of glycosuria for years, perhaps for the duration of their lives, observing the changes in the blood and tissues from time to time, we might gain more information about the mechanism by which the degenerative lesions occur than has been possible in studies of clinical material.

We have proposed, and indeed have begun, to render a good many dogs diabetic with alloxan, perhaps 100 if we can, and to divide them into two groups, one of which will be kept as nearly free of glycosuria as possible with insulin, the other being allowed to run far out of control. Half of each group will be on a high carbohydrate–low fat diet and half on a low carbohydrate–high fat diet in an effort to determine whether hyperglycemia and hypercholesteremia favor the development of degenerative complications.

Fundamental in any consideration of diet and insulin in the treatment of diabetes is the question of what we as physicians are trying to accomplish. Do we want to control glycosuria as completely as possible, consistent with the avoidance of hypoglycemia? Or are we to be content with allowing patients to eat much as they please, excreting large amounts of sugar in the urine, as long as they do not have thirst and polyuria, and taking only enough insulin to avoid ketosis?

It is self evident, I trust, that if the latter point of view is adopted, any discussion of diet is meaningless. There is no diet, in the usual sense, and the problem of insulin becomes negligible.

My personal views on the subject may be summarized as follows: If no one has proved that persistent hyperglycemia is harmful (and I may say that there is excellent evidence of harm in animals), neither has any one, including the advocates of the free diet, proved that it is not. Until such proof is at hand, it will be unwise and unsafe to abandon attempts to keep the blood sugar reasonably close to normal. I will be the first to admit that in the young unstable diabetic person that goal is often difficult, if not impossible, of attainment without running the risk of a more immediate and serious danger, that of severe hypoglycemic reactions. In such situations one is forced to compromise with principles. The dose of insulin must be adjusted so that hypoglycemia never occurs, and this, in the unstable cases, means inevitably, though none the less regrettably, considerable glycosuria some of the time.

Important aspects of a diabetic diet are:

1. Establishment and maintenance of normal nutrition
   (a) If patient is too fat, reduce him
   (b) If patient is to lean, fatten him, slowly
2. Calories (these are considered before carbohydrate, protein and fat):
   Basal, 20 to 25 calories per kilogram (10 per pound) of standard weight
   Add 30 per cent for sedentary workers
   Add 50 per cent for more active persons
   Add 100 per cent or more for laborers
3. Protein (1 Gm. per kilogram [½ Gm. per pound] of body weight)
4. Carbohydrate and fat (one-half the remaining calories [total calories minus protein calories] in each)
   Low carbohydrate diet only for new patients not already receiving insulin
5. Minerals and vitamins

A diet for an office worker (moderate activity) whose both actual and ideal weights are 70 Kg. might be calculated as follows:

Body weight	70 Kg.
Basal caloric requirement (70 × 20 calories)	1,400 cal.
Add 50 per cent for moderate activity	700 cal.
Total caloric requirement	2,100 cal.
Protein allowance (1 Gm. per kilogram)	70 Gm.
Protein calories (70 × 4 calories)	280 cal.
Balance to be supplied by carbohydrate and fat	1,820 cal.
Carbohydrate calories (1,820 ÷ 2)	910
Carbohydrate grams (910 ÷ 4)	228
Fat calories (1,820 ÷ 2)	910
Fat (910 ÷ 9)	110 Gm.
Final diet prescription	
Carbohydrate	228 Gm.
Proteins	70 Gm.
Fat	110 Gm.

Carbohydrate may be distributed, percentage wise, between the three principal meals and a bedtime feeding in some such proportion as 20-35-35-10.

It is necessary to emphasize to the patient the importance of the quantities as well as the kinds of food, the constancy of carbohydrate intake from day to day and the ability to make simple substitutions to avoid monotony and yet keep constancy.

Four types of insulin are now available: soluble or "regular,"[1] protamine zinc, globin and mixtures of these prepared by the physician or the patient.

The figure shows the various blood sugar time curves obtained with these different forms of insulin. All of the curves were obtained for the same diabetic patient on different days, with a constant regimen which consisted of the patient's receiving feedings of milk every two hours throughout the twenty-four hour period. This was to insure that his state of hydration and nutrition would be constant and unvarying throughout the observations. On one of the days he was given a dose of 35 units of protamine zinc insulin, and his blood sugar went up a little for almost four hours, then gradually went down, until at the end of twenty-four hours it had reached its lowest point. In contrast to protamine zinc insulin, regular or crystalline insulin, given in exactly the same dose, reached its peak of activity at six hours and gradually tapered off, so that at the end of fourteen or sixteen hours the level of blood sugar had returned to its initial

Read at the interim meeting of the American Medical Association, Cleveland, Jan. 8, 1948.
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1. The manufacture of crystalline insulin (solution of zinc insulin crystals) is being discontinued.

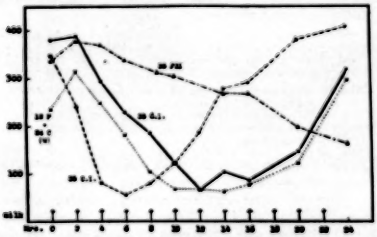
point. If regular insulin and protamine zinc insulin are combined, are mixed in the syringe in the proportion of 2 parts of regular to 1 of protamine zinc insulin, one secures a curve which is, on the whole, intermediate between that of protamine zinc insulin and that of crystalline or regular insulin alone. It is interesting that this type of curve closely parallels the curve produced by globin insulin in a similar total dose.[1]

These four types of curves, then, can be taken to characterize the action pattern of the different types of insulin now in common use.

With reference to protamine zinc insulin, it should be emphasized that the curve shown in the figure is that which is obtained only after a single test dose of the substance.

Protamine zinc insulin, when given daily, at twenty-four hour intervals, has an entirely different type of activity.

Soon after the discovery of protamine zinc insulin, it began to appear from clinical results that its activity was relatively constant throughout the twenty-four



Blood sugar time curves for a diabetic patient obtained with different forms of insulin (Ricketts, H. T.: Certain Aspects of the Newer Insulins, Illinois M. J. 87: 133 [March] 1945). The vertical column of figures at the left shows the number of milligrams of sugar in the blood per hundred cubic centimeters.

hour period. To put this probability to the test, we devised the plan of giving protamine zinc insulin to a diabetic patient first in the morning for several days, testing his blood sugar four times each day, averaging the results and plotting them as a curve. We then gave it to him in the evening for several days, getting a similar series of figures and finally checking again with another morning series represented by still another curve.

It was reasoned that, if protamine zinc insulin had a fairly constant activity throughout the twenty-four hours, then the shape of the blood sugar curve should not be altered, no matter whether the patient received his insulin in the morning or in the evening; the curve ought to be reproducible. If the activity of protamine were not constant, if there were, in fact, a period of maximum activity and then waning activity, as there is with a short-lasting insulin, then it should make a good deal of difference whether one gave the protamine zinc insulin in the morning or in the evening.

It will be apparent, I think (from the curve) that there is little difference except at one point between the results of morning and of evening administration of protamine zinc insulin.

A similar type of observation was made on another patient. Again, the averages were plotted of several days' determination, not of a single day; it was apparent that the action of protamine zinc insulin is the same, whether it is given in the morning or in the evening.

Now, in order to establish that if a short-lasting insulin were given in the morning as against the evening the curves would be different, other curves were obtained. Regular insulin was now given for some time in the evening, with one type of curve resulting. Regular insulin was then given in the morning, with the other type of curve resulting. Finally, the patient was given no insulin, and a curve was obtained which was similar in shape to the curves produced by protamine zinc insulin. This constitutes further evidence that the activity of the protamine zinc insulin is a relatively constant matter. It simply lowers the general level of the blood sugar.

If protamine zinc insulin does, in truth, act fairly constantly throughout twenty-four hours, it helps one to understand why it is not able to take care of the food intake in persons with severe diabetes, in whom the pancreas is unable to produce a little insulin in response to the ingestion of food. It explains, on the other hand, why protamine zinc insulin is effective in persons with mild diabetes, who have a good pancreatic reserve.

These differences in the effectiveness of protamine zinc insulin from one type of patient to another are illustrated by curves obtained for persons with diabetes of varying degrees of severity before and after partaking of food. It is apparent that in each case protamine zinc insulin controls the fasting blood sugar very well. The postprandial blood sugar, however, is well controlled only in the milder cases, and the severer the diabetes the less successful is this preparation in returning the blood sugar to normal two or three hours after a meal. Such failure is most pronounced in the most severely diabetic subject we know of, the totally depancreatized dog.

In patients with severe diabetes, therefore, protamine zinc insulin must be supplemented by a quickly acting insulin if the blood sugar after meals is to be kept within reasonable limits. This type of insulin (regular or crystalline) is given at the same time as the protamine zinc insulin, before breakfast, and may be administered either separately or as a mixture. It must not be forgotten, however, that the effect of a dose of regular insulin given separately is different from its effect when mixed with protamine zinc insulin. In the latter case a considerable proportion of the regular insulin is converted to the protamine complex by the excess of protamine present.

Dr. Colwell of Chicago, Dr. Peck of Indianapolis, Dr. McBride of St. Louis and Dr. Wilder at the Mayo Clinic have been actively concerned in the use of insulin mixtures in the syringe. One of the advantages is that, in place of having to give two injections of insulin to the severely diabetic patient, whose disease protamine zinc insulin alone will not control, one can add a quickly acting component to the mixture and accomplish about as much in one injection as could be accomplished in two separate injections of crystalline and protamine zinc insulin.

It has been observed by the majority of investigators that a mixture consisting of 2 parts of crystalline or regular insulin to 1 part of protamine zinc insulin fulfils the requirements well for the vast majority of diabetic patients, perhaps 80 or 85 per cent. One must not, however, forget the remaining 15 or

20 per cent, in whom a different proportion of regular to protamine zinc insulin may be necessary. The advantage of using mixtures is precisely that one can change the proportion of one to the other, as the requirements vary from patient to patient or in the same patient from one time to another.

The diagrammatic representation of Colwell's data indicates the action of regular insulin, protamine zinc insulin and 2 to 1 crystalline to protamine zinc insulin mixture, the action of which lasts less long than that of protamine zinc insulin and begins less abruptly than that of regular insulin. The action is also shown for a 3 to 1 mixture of crystalline to protamine zinc insulin. It must be apparent that, as one increases the proportion of crystalline insulin in a mixture of crystalline and protamine zinc insulin, the onset of action of the insulin is accelerated, with less duration of action.

The principal point, to be made is that by altering the proportion of one type of insulin to the other, one can obtain a type of compound to suit the individual needs in the vast majority of instances.

If air is not injected into the bottle at the time the insulin is withdrawn a vacuum is produced which makes manipulation difficult. Therefore, one ought to inject into the bottle the same number of units of air, so to speak, as of insulin withdrawn from the bottle.

A comparison of globin insulin with other forms of insulin is illustrated in a young girl with relatively severe diabetes. Crystalline insulin given morning and night (12 units each time) led to an extremely high level of blood sugar on arising, which is characteristic of severe diabetes in young persons. The crystalline insulin kept on working all day, and the low point showed that there was a tremendous change in the level of the blood sugar.

Globin insulin given in the same total dosage produced considerably better results and in this case, obviously, had an action which lasted more than twenty-four hours, or at least twenty-four hours, because the fasting blood sugar was much better than with two doses of crystalline insulin per day (breakfast and supper).

A comparison was made of the effect of globin insulin with crystalline insulin alone in a patient with milder diabetes. From the curve for globin insulin and the curve for crystalline insulin, it was apparent that the crystalline insulin, a short-lasting insulin, does a better job in this particular patient than did the globin type. It is not always the case.

In another patient globin insulin obviously failed to have a twenty-four hour effect. Any variation from marketed protamine zinc insulin should have, in my opinion, the minimum requirements of full twenty-four hour activity in all patients, not in some but in all. Unless that criterion is fulfilled, there is little excuse for adopting a long-lasting insulin other than protamine zinc insulin.

Efforts are under way to secure a stable preparation with a shorter duration of activity than that of protamine zinc insulin and a quicker onset of action, and the preparations which we have tried so far have all had twenty-four hour activity in all patients. That, I think, is important. Globin insulin does not have twenty-four hour activity in many patients, and that is one reason that I do not advocate its routine use.

The practical application of the technic of adjusting the patients to diet and insulin can be represented by charts. In the patient with mild diabetes, our custom, if we have not observed him before, is to give him a diet containing 100 Gm. of carbohydrate distributed equally among the three meals. If, with such a regimen, the patient returns in a week with a record of urinary tests showing that the condition was not controlled with diet alone, a small dose of protamine zinc insulin is prescribed, and since insulin must be taken anyway, the carbohydrate intake is increased to a more nearly normal figure. With mild diabetes, such a maneuver is almost uniformly successful.

If the diabetes is severe, there is a different problem. Treatment of the previously untreated diabetic person is started with 100 Gm. of carbohydrate per day. If at the end of a week it is obvious that insulin is needed, the diet is changed to include 150 or 200 Gm. of carbohydrate. He is given 10 to 20 units of protamine zinc insulin. Protamine zinc insulin in adequate amounts will usually be observed to control the fasting urine specimen.

When one gives the same total dosage in a mixture of 2 to 1, one is likely to effect considerable improvement in results of urinary tests, which can be still further improved, perhaps, by juggling the amounts of carbohydrate among the various meals.

I would like to end on the note with which I began, that my colleagues and I are not yet ready to abandon the goal of careful control of the blood sugar in the treatment of diabetic patients.

ABSTRACT OF DISCUSSION

ON PAPERS BY DRS. WILDER, PALMER AND RICKETTS

QUESTION: Why is it they have so many more men with diabetes at the Mayo Clinic than they do women?

DR. WILDER: There is about an equal number of men and women in the Mayo Clinic. Most statistics on diabetic deaths indicate the presence of more women than men. Most diabetic surveys or at least most complications of diabetic incidence have indicated more women than men. Why our figures were different from those of almost every one else has been a puzzle to us for many years. This has been going on year after year for the last twenty years, at least, with, I will say, 51 or 52 per cent of men and 48 or 49 per cent of women, rather than the reverse in other places. We have felt that perhaps we were getting more accurate figures on sex incidence than Dr. Joslin was, because persons that we see do not come to us because they have diabetes. We have no Dr. Joslin in the Mayo Clinic. They come for everything else under the sun. They are all examined carefully, no matter what the matter is with them. Sugar, when it is found, is followed up by examinations of blood. That has given us our figures. I am interested that Dr. Wilkerson's figures at Oxford, Mass., where, again, everybody was examined, not only those who happened to come because they had diabetes, show a close incidence of men and women. It is true that women outnumber the men a little, but the degree is so small that I wonder whether it really has statistical significance. Likewise in Stockholm, where they recently had a survey of the incidence of diabetes, based on applications for special rations during the war—there was an incentive for these men to present themselves for examination—the incidence of men in most of the decades exceeded that of the women, just as it does with us.

QUESTION: How does the intravenous glucose tolerance test compare with the oral?

DR. WILDER: In the intravenous test one gets a sharper rise, of course. I imagine it is equally useful, provided that one had a mass of experience with it so as to be able to compare the finding in an individual case with the general finding.

QUESTION: Do you use oral glucose generally?

DR. WILDER: We use the oral test exclusively.

QUESTION: Do you consider the "clinitest" reliable for patients to depend on for urine test?

DR. WILDER: We are using the "clinitest" right along in most patients. We teach them the Benedict qualitative test and the "clinitest." They must be urged to keep these tablets from deteriorating, by keeping the bottle tightly closed. When they deteriorate, the patients may be led astray and think that they have different amounts of sugar than they have. However, mistakes also are made with the Benedict test. I had 1 patient who died as a result of diabetic acidosis, led astray by buying Benedict's quantitative solution rather than Benedict's qualitative solution and failing to get a reaction that he recognized as positive.

QUESTION: Please explain how a drop of arterial blood is used in determining diabetes.

DR. E. P. JOSLIN, Boston: Mrs. Leech in our exhibit is determining blood sugars by taking a drop of blood from the ear. There was one thing which I could tell Mrs. Leech today that encouraged her. One of the men formerly working with us, and now in a fairly large city, the other day saw a patient evidently going into acidosis, as he thought. No opportunities for determining blood sugar were available, even in this large city. The physician happened to remember Mrs. Leech's test, carried it out himself, and determined the patient's blood sugar, 600 mg., and the patient came out of coma.

QUESTION: What method of determination of blood sugar do you suggest as being simple but accurate for the doctor who must do his own office blood sugar determinations?

DR. WILDER: I think that this technic which Mrs. Leech is developing is going to be the answer to that question.

DR. HUGH L. C. WILKERSON, Boston: We are conducting a program in diabetes control in two parts of the country, one in Brookline, Mass., where we are doing case finding and general educational work with the public, and also some educational work with diabetic patients. In Jacksonville, Fla., we have a program in diabetics, not just a survey, where we are doing case finding and education of the patient. In particular, we are holding classes for diabetic patients referred to the health department by practicing physicans for education. These educational classes are conducted by nurses and nutritionists who have been specially trained in diabetes. We have a series of lectures given by a doctor not in practice, a health officer who has had considerable training especially in diabetes. We also have a register of diabetic patients, now more than 800 in number, which has been compiled by the practicing physicians referring their patients to us for contact purposes, to get the names of their relatives and for other purposes of education.

We find that we are getting many more than 2 per cent of the relatives of diabetic patients who actually have diabetes. More than 1 per cent of them have not formerly known that they had any signs or symptoms of the disease. In addition to that, we are doing research work on simplified procedures for diagnosis. We are also preparing for the use of the general practitioner and for health departments, valuable, simple educational material.

DR. JOSLIN: Dr. Palmer brought out what has been emphasized by Dr. McCullagh and others today, that the adequate treatment of diabetes, the aggressive treatment of it, results in a smaller number of complications.

QUESTION: Will you discuss the intravenous use of ether in diabetic gangrene?

DR. PALMER: I know Dr. Katz of New Orleans, and I know he is enthusiastic about it. I have talked to many men who have used it. If one can follow the patients, it is a temporizing measure and may be helpful. I would not condemn it, and I do not encourage its extensive use.

QUESTION: Do you use heat or cold in wet diabetic gangrene, while using antibiotics before resorting to surgery?

DR. PALMER: You should be careful of heat in all cases of diabetes. In the past we have used more heat than at present. I think we try to maintain not cold temperatures. I do not apply refrigeration at all in the attempt to control sepsis from an extremity, unless I were going to use that as the anesthetic.

DR. PALMER: We have used considerable rutin. I cannot be too enthusiastic about it; it is all right to use it.

DR. JOSLIN: About the rutin, Dr. Dodger recently, in his careful article in THE JOURNAL, was rather pessimistic. I think our group is not so pessimistic as that. They are rather open-minded. Dr. White feels that with the children who have used rutin the progress of the disease in the eyes has been less rapid. I would like Dr. Wilder to say a word on rutin.

DR. WILDER: We have used it on a good many cases, with results that we cannot interpret. There are some cases of untreated retinitis in diabetes that get spontaneously better. Those cases that have gotten better under the administration of rutin may have deceived us. We have at present an impression —it is nothing more or less than a clinician's impression—that some of these cases have been arrested, their progress delayed by the use of rutin. This is exactly the same impression your associates apparently have in Boston.

QUESTION: Do you plan your diets at all as to the content of cholesterol?

DR. RICKETTS: We do not. Perhaps we should but we have not paid much attention to that. One thing that makes me say so is the report from Rabinowitz' laboratory and clinic in Montreal, in which he had patients, some on high cholesterol and some on low cholesterol diets, and the difference between the blood cholesterol in the two groups was slight. I have never been convinced that it was real or important.

QUESTION: Will you kindly repeat your method of determining the amounts of protein, carbohydrate and fat in the diet?

DR. RICKETTS: One gives 1 Gm. of protein per kilogram or approximately that. If the total caloric requirement is 2,000 calories, one gives, then, 75 Gm. of protein to a man weighing 75 Kg. He supplies in that protein 300 calories, 4 times 75. Subtracting 300 from the 2,000, which we allow, leaves 1,700 calories to be supplied in protein and fat. Of this 1,700 calories, 850 ought to come from carbohydrate and 850 ought to come from fat. If the carbohydrate calories are to be 850, that is equivalent to approximately 210 Gm. of carbohydrate in the diet and 850 calories of fat is equivalent, roughly, to 90 Gm. of fat.

QUESTION: Do you feel it necessary to hospitalize a patient while stabilizing on diet and insulin?

DR. RICKETTS: Ordinarily not.

DR. JOSLIN: It seems to me that we are treating more and more in the office, just as the surgeons more and more are doing preliminary work before they send the patients to the hospital. Really, we have to thank the Mayo Clinic for driving that home, because they have all sorts of dining rooms and they have treated many diabetic persons that way. We know that they do save their hospital beds. We learned a great deal.

QUESTION: At what intervals during the day do you do a quantitative determination of sugar in the urine?

DR. WILDER: In our clinic we do quantitative tests only on twenty-four hour collections and that infrequently. We feel the qualitative test is sufficient for tractions during the day.

QUESTION: How would you aggressively treat a patient with mild diabetes who has a fasting blood sugar of 130 to 140 mg., with no symptoms?

DR. WILDER: It would depend a good deal on the patient, of course. If it is an overweight person, probably the best treatment for him would be a diet without any insulin at all. He probably can be treated with diet, without any insulin, under any circumstances. If it is an early case, I would be much more inclined to be rigid in my management than if it is a later case, because the earlier cases are the cases in which a rigid management can be expected to do some good. After diabetes has lasted two or three years, it has reached a degree of severity that it is likely to continue from then on throughout life. It will be aggravated by infections but it will come back after the infection is over to about the degree of severity it had before. It was just before I left home that I saw a woman who has had diabetes thirty years. She was 50 years old, was only 20 when it started. Our patients starting diabetes at 20, with the typical triad of symptoms, nearly all require insulin. This woman had not used insulin all her life; she had had diabetes thirty years and still was what we call a grade 2 diabetic. When she overstepped the diet, her blood sugar went up to 300 to 400 mg. When on careful diet, she was all right.

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Special Article

CANCER OF KIDNEYS, ADRENALS AND TESTES

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This article is the sixteenth and last of a series to be published by the American Medical Association in cooperation with the American Cancer Society. The series is designed to aid in the early diagnosis of cancer and thereby to gain more effective results in treatment.

CANCER OF THE KIDNEY

In two periods of life cancer of the kidney occurs, in infancy and in aging adult life. In infancy occurs one of the more frequent cancers of childhood, Wilms' tumor or infantile embryoma. This is a silent tumor and is highly malignant, with a serious and impressive record of fatal termination. More frequently, there occur in middle-aged or in elderly persons the various epithelial carcinomas of the kidney which are often silent until they reach considerable size and usually show their presence by blood in the urine. The early recognition of renal cancer in both these age groups is a problem for the medical practitioner, because by early surgical removal of the affected kidney lies the correction of an otherwise fatal course of the disease.

Carcinoma of the kidney ranks third in frequency among the tumors of the urogenital system, following carcinoma of the bladder and of the prostate A few rare tumors of the kidney, not epithelial in origin, such as fibrosarcoma and leiomyosarcoma arise from the renal capsule or pericapsular tissues. The usual cancer is one epithelial in origin, originating from the renal parenchyma or from the epithelial lining of the pelvis. The latter, a specialized epithelium, is in the lining of the ureter and bladder, and all the tumors arising from this specialized epithelium are of similar class, whether from renal pelvis, ureter or bladder. The tumors occurring from the renal parenchyma itself are specific tumors of that tissue.

The formation of the renal parenchyma is of two origins: (1) the part formed from the renal blastema is that part above the "connecting piece" in the system of Henle and (2) the portion below the connecting piece is from the wolffian system and actually is of the same embryologic origin as are the renal pelvis and the ureter. The separate origin of the two parts of the renal parenchyma would lead one to suspect that two different types of tumor cells would occur. Two different types of tumor cells do occur, one a clear cell and the other a granular cell. One or the other may be the predominant cell in a tumor, or sometimes a part may be of clear cells and another part of granular cells. There is, however, as yet no acceptable evidence as to the origin of either the clear cell or the granular cell except that they both are undoubtedly of renal origin. It is also true that clear cell carcinomas occur more frequently in the cortical areas and granular cell tumors more often in the medullary and corticomedullary areas. The clear cell carcinoma may originate from the renal blastema cell; its growth action to some degree suggests such origin, and the granular cell arising from the wolffian system resembles the infiltrating carcinoma of that system.

Small cortical adenomas of the kidney, entirely symptomless, are not infrequently found at operation or at autopsy. These small encapsulated adenomas are considered benign; they may be microscopic in size, and whether they play any part in the production of carcinoma of the kidney is uncertain.

The classification of renal tumors like tumors elsewhere has at times little agreement between clinicians and pathologists. Two recent studies of large series, one by Fite [1] and the other by Melicow,[2] have considerable classification in common. First, pathologists agree that most renal tumors are renal in origin and that the old term "hypernephroma" if used should be reserved for that small class of adrenal rest tumors.

The following simple classification of renal parenchymal tumors has been found most useful: *(a)* clear cell carcinoma; *(b)* granular-cell carcinoma (some tumors occur in which both types of cells occur without evidence as to which one was primary or secondary); both types of cell tumors may show alveolar, adenomatous, tubular, papillary or cystic formations, which are normal or abnormal anatomic architectural arrangements of renal cells; *(c)* true hypernephroma (adrenal rests); *(d)* tumors in solitary cysts; *(e)* multiple papillary adenoma or carcinoma in sclerotic tubular cysts, and *(f)* mixed forms, among which the carcinosarcoma of infants (Wilms' tumor) is the most frequent.

PARENCHYMAL RENAL CARCINOMA

Parenchymal renal carcinoma is a disease of middle age. In 182 successive cases it occurred in the following ages: 20 to 30 years, twice; 30 to 40 years, sixteen times; 40 to 50 years, forty-two times; 50 to 60 years, sixty-four times; 60 to 70 years, thirty-eight times, and 70 to 80 years, twenty times.

Carcinoma of the kidney occurs more frequently in the male, in the ratio of 3 to 1. In females when tumor occurs it has been most often subsequent to the menopause. The carcinoma occurs about equally on both sides, but has been more frequently operated upon on the right side. Inoperable tumors, due to size fixation or with metastases, occur more frequently on the left side. In the 182 cases mentioned, no operation having been performed because of pulmonary metastases in 24 cases, there were 20 cases with tumor of the left kidney and only 4 with right-sided tumor. A plausible reason assigned was that the deeper situation of the left kidney was more often associated with delayed recognition of the disease, as well as the fact that hematuria occurred more often with right-sided tumors than it did with tumors of the left kidney. Bilateral tumors are rare, occurring once in about 100 cases.

Symptoms.—The symptoms of parenchymal renal carcinoma are a triad of hematuria, pain in the flank and a mass in the flank.

Hematuria occurs in over 70 or 80 per cent of the cases; it presumes a vascular rupture in a well developed neoplasm and should be a late symptom of tumor growth. It is the most frequent and the most important symptom. It may be entirely painless, and sudden in its appearance, and it may spontaneously disappear, or the bleeding

1. Fite, G. L.: Classification of Tumors of the Kidney, Arch. Path. 39:37, (Jan.) 1945.
2. Melicow, M. M.: Classification of Renal Neoplasms: A Clinical and Pathological Study Based on One Hundred and Ninety Nine Cases, J. Urol. 51:333, 1944.

may last a variable time, then cease, and may or may not recur later. At times it may be associated with renal colic, and the patient may pass blood clots. The clots may be like ureter casts. The bleeding is apt to be total and the same throughout the urine until it ceases, to recur later. In some cases the bleeding may persist until corrected by surgery. There is nothing specific about the hematuria that separates renal bleeding from ureteral or vesical.

Pain may occur as a dull ache in the flank. It may be associated with hematuria. At times it may be severe, typical of renal colic, and then definitely associated with passage of blood clots. Continuous fixed pain in flank or back may be a symptom seen with large tumors.

A mass in the loin or a palpable mass in the renal region is frequently found at the time of the appearance of the hematuria. In almost 10 per cent of the cases the patient is conscious of the mass himself. In over 60 per cent of the cases presenting with hematuria, a renal mass was palpable on the first examination. This usually is felt bimanually and is associated on palpation with deep inspiration.

The three symptoms hematuria, pain in the flank and a palpable mass in the flank are frequently the only symptoms present in the early onset. Other symptoms may then follow. Urinary difficulties may arise due to a blood clot in the bladder, and since most of the patients are elderly men, coexistent prostatic hypertrophy may be present with urinary frequency and lessened stream.

Weakness and loss of weight become more frequent as the disease progresses. Often the weakness is present as an only symptom, and at times it seems to be directly associated with the specific tumor and not with metastases, as the weakness syndrome often disappears a few days after the tumor is removed surgically. Fever is not infrequently seen with renal carcinoma. In a few cases unexplained fever was the only presenting symptom. When fever occurs it has been attributed to intratumor hemorrhage and subsequent necrosis, and later often in such cases calcified deposits in the tumor are seen in roentgenograms.

When metastases occur, the symptoms are referable to the organ involved. Rarely the first symptom may be that of metastases. This may be seen with spontaneous fracture of a long bone or the finding of metastases in the lung by roentgen ray. Metastases are found in about 30 per cent of the cases when first seen on admission. About 50 per cent of these are seen in the lungs; about 20 per cent are in the bones. Metastases occur next in frequency in the liver and in the brain.

CLEAR CELL CARCINOMA

The clear cell carcinoma, the most frequent type of tumor seen, was formerly described as hypernephroma by Grawitz, and was supposed to be an adrenal tumor, but it is now generally accepted that it is entirely renal in origin. This tumor grows slowly, may or may not be partially encapsulated, projects as a mass out from the cortex or intrudes on the pelvis. The tumor is soft, with large spherical masses, yellow in color, vascular within and without the tumor, and it may remain local, growing slowly for a variable length of time. Years may pass before the tumor breaks through its barriers and spreads. When it does it may spread locally through the capsule or may form large thrombotic masses which protrude into the veins, at times into the renal vein and vena cava, and which then appear as spherical metastases in the lungs. The most usual place of metastases with clear cell carcinoma has been in the capillaries of the lungs. This tumor also has a "selective tendency" to metastases

Fig. 1 (M.F.).—A retrograde pyelogram of a clear cell carcinoma of the left kidney. It shows that the tumor mass growing in the upper pole has elongated and twisted the upper calyces and obliterated part and has displaced the renal pelvis and lower part of the kidney downward.

to bone, long bones most often. The clear cell carcinoma is seen among an earlier age group than the granular cell carcinoma.

GRANULAR CELL CARCINOMA

The granular cell carcinoma, the next most frequent type of renal cancer seen, is a more rapidly growing and a more malignant carcinoma than the clear cell. It occurs more frequently in the older age group. It forms a hard solid contracting type of tumor much less vascular then the clear cell but, being more invasive, is more frequently seen with hematuria (80 to 90 per cent) and with pain. This tumor is often stony hard in the kidney and resembles the undifferentiated carcinomas elsewhere, extending by direct extension, by the lymphatics and by the blood stream. Metastatic involvement of preaortic lymph nodes and mediastinal nodes is not infrequently seen early with granular cell carcinoma.

Tumors occur in which both types of cells occur, a mixed cell type. Part of the tumor will be of large soft yellowish masses, but other portions will be hard, nodular and fixed. Examination will show clear cells in one and granular in the other. There has been no evidence as to which type may have been the primary, but these tumors in progress and in seriousness resemble more the granular cell tumor than the less malignant clear cell tumor.

From a consecutive series of 100 cases of all types of parenchymal tumors, the following symptoms occurred: hematuria, 85 cases; loss of weight, 60 cases; intermittent pain in the flank, 30 cases; fixed pain in the back, 22 cases; a palpable tumor (noted by the examiner), 46 cases; a mass as a complaint, 8 cases; weakness or fatigue, 22 cases; difficulties in voiding urine, 12 cases, and fever, 9 cases.

The finding of varicocele on the same side is not infrequent. If pronounced, it is often found to be

associated with an obstructive thrombotic tumor mass in the renal vein.

DIAGNOSIS

It is now an accepted axiom that all cases of hematuria require a urologic investigation as to the source of the hematuria and its cause. Since

Fig. 2 (M.G.).—Retrograde pyelograms in a case of granular cell carcinoma of the kidney, showing contraction of the hard dense renal tumor so that the calyces are almost completely closed. The renal tissue also shows a denser shadow than normal.

the widespread use of intravenous pyelographic mediums, a recognition of the alterations of renal anatomy and physiology suggestive of tumor is more definitely widespread. However, experience has shown most urologists that useful as are intravenous secretory pyelograms, they do not offer the criteria obtained by cystoscopy and retrograde pyelograms. Thus in all cases of hematuria, unless the cause is definitely ascertained by ordinary roentgenograms or intravenous urograms, and if a tumor is suspected, there should be a complete cystoscopic examination. The cystoscopy done at the time of hematuria establishes the site of the lesion, the secretory change on the suspected side compared with the normal, or the proof that the opposite kidney functions normally. The retrograde pyelograms give clearer delineations of the internal architecture of the renal system, far superior to secretory urograms. Often when a tumor is present, with destruction of the renal parenchyma there are insufficient secretory mediums into the pelves and calyces for an interpretive pyelogram with secretory mediums.

Studies of the pyelograms with the types of renal carcinoma have shown the various changes. Large tumor shadows are seen with elongated, narrowed and in other places dilated spidery-shaped calyces spreading beyond a normal renal area; these are characteristic of the clear cell carcinoma. The shadows at times resemble those seen in the pelves and calyces when the kidneys are polycystic. Some resemble the shadows seen with solitary or simple cysts and, since these are often unilateral, may make a specific diagnosis difficult. Narrowing or obliteration of the calyces as shown by the roentgenograms —in fact, in some cases complete disappearance of calycine shadows, with only a compressed pelvic shadow present, are the appearances associated with the granular cell type of carcinoma. In some cases there appear areas of the large spreading spidery calyces, and in others the obliterated or pinched calyces; this type of roentgenogram is more often seen with the mixed type of tumor. Studies made of kidneys after removal support the interpretive diagnosis in large series of these cases. Hemorrhage is not infrequent within the tumors themselves, and with subsequent necrosis there are deposits of calcified material at various parts of the tumors, so that calcified areas, either small or large, are present in about 25 per cent of the cases and are shown by roentgenograms.

Cytologic examination of the urine is of importance in these cases, as has been stressed by Papaniculaou.[3] This may be of the gross urine or may be of material from the ureteral specimens. The examination in which the sediment is fixed and mounted as tissue requires experience as to interpretation because of the changes occurring in the cells which are due to immersion in the urine. In parenchymal tumors, two types of cells are seen: (1) unusually large cells with irregular or multiple nuclei, especially cells with mitotic changes and (2) vacuolated cells with clear cytoplasm, rich in lipids, so characteristic of clear-celled carcinoma (hypernephroma). With experienced observers the high proportion of cases in which these cells are found and the accuracy of their diagnosis are astounding. The use of cytologic studies in all urinary tumors is an essential step, particularly when diagnosis is difficult.

THERAPY OF PARENCHYMAL CARCINOMA

Early surgical removal of the involved kidney and capsule is the only known corrective procedure for renal parenchymal carcinoma. Although recession in size of some renal carcinomas has been reported as a result of roentgen therapy, the resistance of these cancers to roentgen therapy is well known, and any temporary recession of the tumor mass is largely the effect of the radiation on the smaller blood vessels. Because such radiation takes a number of weeks to administer and its effect may be doubtful, preoperative radiation is not widely used for renal carcinoma. In addition, there is difficulty in wound healing and a higher proportion of wound disruption following the operation. These in themselves would not be insurmountable difficulties if there were assurance of the effectiveness of the radiation on the tumor cells, but any effect with the radiation at present administered is questionable. With absence of demonstrable metastases, all renal tumors should, if possible, be completely extirpated as soon as recognized. The major difficulty lies in earlier recognition. Even with questionable metastases, removal still offers the only possible chance with the therapeutic agents now at hand. The size of the tumor mass is no contraindication; although size may be an indication of the duration of a tumor, it is not a definite indication of its activity. Often large tumors may be of low grade malignancy and of slow extension. Theoretically ligation and division of the renal vessels are the ideal first steps in surgical removal of a tumor. This may be more simply accomplished by transperitoneal approach. It may also be done effectively through the flank. The

3. Papaniculaou, G. N.: New Procedure for Staining Vaginal Smears, Science 95: 438, 1942; Tr. Am. A. Genito-Urin. Surgeons 38: 147, 1946.

approach, whether flank or abdominal, should be large, much larger than the tumor, so that after ligation and severance of the vessels, the tumor, kidney and perinephritic fascia may be removed en masse with a minimum of trauma. Since parenchymal tumors rarely, if ever, metastasize down the ureter, it is only necessary to remove the accessible portion. Examination of the removed organ will often show extension of tumor into minor or major veins; hence handling of the mass should be at a minimum and severance of the blood vessels should be the first step. Tumor masses may extend into the renal vein and vena cava. Such should be removed from these vessels with religation after removal, experience having shown that at times tumors do not recur in such cases. Retroperitoneal masses of lymph node involvement may be present. These are more frequently seen with the granular cell and mixed cell tumors and are usually discovered after the renal tumor mass is removed. When these nodes are found they may be removed, but rarely has it been possible to do so completely.

PROGNOSIS AND RESULTS

The clear cell renal carcinomas have a much higher percentage of freedom from recurrences than do the granular or mixed tumors. The clear cell tumors, even though of large size, when removed without dissemination show in the various clinics a freedom from recurrence over a five year period varying from 25 to 50 per cent. The freedom from recurrence with the granular cell tumors is much lower, varying from 5 to 10 per cent. Cases of demonstrable metastases treated by roentgen rays without nephrectomy or after nephrectomy show an extremely low survival rate; most patients do not survive a year. Rarely a solitary metastasis may occur and be successfully removed with a good survival rate. Even solitary pulmonary metastases have been successfully removed in clear cell carcinomas with apparently no further recurrence. Improvement in the figures of recurrence is occurring largely as a result of earlier recognition of the disease and widespread improvement in diagnostic procedures. Earlier investigation of those with suggestive symptoms is necessary because even in the most accessible clinics symptoms are present at least a year on the average before the diagnosis is made. It will be interesting to observe the effect of the establishment of the cytologic test of a urinary smear as advocated by Papanicolaou in the routine of laboratories, in the hope that these cases will be reached by therapy earlier in the disease, for therein lies the path of improvement.

CANCER OF THE RENAL PELVIS

Carcinoma of the renal pelvis, arising from the specialized epithelial lining, is the same as the epithelial cancers of the ureter and the bladder. They are less frequent than parenchymal tumor, occurring in the Squier Clinic in a ratio of 1 to 8 (22 to 160). They occur in both sexes, slightly more frequently in males, and occur equally in either kidney. They are more apt to occur in the elderly age group. The decades are 30 to 40 years, 1 case; 40 to 50 years, 3 cases; 50 to 60 years, 7 cases; 60 to 70 years, 6 cases, and 70 to 80 years, 5 cases.

Recognizable etiologic factors may have some influence on the formation of this tumor. Certain aniline dyes with carcinogenic factors have been known to produce these tumors, both clinically and experimentally. The linking of these carcinogenic agents with the large number of this type of tumors seen is rare at present because known exposure is rare among the patients seen. Pelvic tumors have been reported as associated with pelvic calculi and with long-standing inflammatory processes. Many authors have emphasized the dangers of neglecting calculi and long-standing infections in the kidney. There does not seem to be any recognizable association with congenital abnormalities themselves in the development of pelvic tumors.

The types of tumors of the pelvis are similar to those of the ureter and bladder. They occur from the specialized epithelium of mesodermal origin. They are classified as (1) papilloma, (2) papillary carcinoma, (3) squamous cell carcinoma and (4) undifferentiated carcinoma.

About 50 to 70 per cent of all tumors of the renal pelvis are papillary. They may be single or multiple and are villous or wartlike growths similar to those

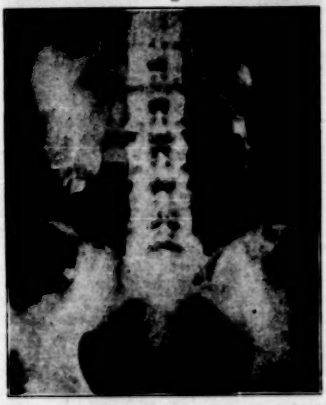

Fig. 3 (J.I.).—An intravenous pyelogram of a papillary carcinoma of the pelvis of the right kidney. The irregular lone dense shadow is seen surrounded by the denser iodide in the urine in the pelvis.

found in the bladder. They may be small or extensive and may be associated with similar tumors in the ureter or the bladder. They are rarely bilateral. These papillary tumors when seen have a higher percentage of malignancy than tumors of the bladder; over 50 per cent of the papillary tumors occurring in the renal pelvis show malignant tendencies. Microscopically the structure of the papilloma is simple and uniform; it consists of a series of branching connective tissue stromas covered with layers of transitional epithelium. When cancerous, they are more compact with invasion of the submucous tissue and with alteration of cell division and abundancy of mitoses; the cells break through the basement membranes. Not infrequently encrustations of urine occur with necrosis of the tumor.

Squamous cell carcinoma in the pelvis is less frequent than the papillary type. It occurs with irritant lesions such as infection, calculus, ureteritis cystica and leukoplakia. The microscopic sections show epidermization and formation of many epithelial pearls. Ulceration is not uncommon, and these tumors are less vascular than the papillary tumors.

Infiltrating undifferentiated carcinoma occurs but

is infrequent. It has the same characteristics as the similar tumors of the bladder; invasion, infiltration, destruction and extension. Tumors of the renal pelvis of papillary type frequently metastasize down the ureter as well as through the lymphatics. Carcinoma most frequently metastasizes through the lymphatics of the renal pedicle and the retroperitoneal nodes. They both then disseminate widely to the lungs, liver, adrenal glands and bones.

Symptoms.—The most outstanding symptom of tumor of the renal pelvis is hematuria. Among 22 cases at the Squier Clinic, hematuria at some time or other occurred in all cases. Other writers have a smaller percentage, but the fact is that this is by far the most outstanding symptom, and it may be the only one. Pain may occur but is not constant nor frequent. If the bleeding is profuse there may be renal colic. If obstruction of the pelvis occurs there may be pain in the flank similar to colic in hydronephrosis. As a rule, however, pain is an infrequent symptom of pelvic tumors.

In only a small number of cases does a palpable tumor mass develop; a concomitant hydronephrosis is the cause of the mass, and this may be relieved by the passage of obstructing material. General symptoms, such as loss of weight, strength and appetite, appear only late in the disease. Vesical symptoms of burning, frequency and dysuria may be present if there is an associated infection.

Diagnosis.—There are no symptoms that are diagnostic of tumor of the renal pelvis. In a case of hematuria and with a complete investigation with cystoscopy and retrograde pyelograms, the condition can be recognized. The defect shadows in papillary tumors may be definitely diagnostic. Not infrequently, obstruction of the ureter may occur, especially with squamous cell carcinoma, and the obstructing lesion produces a characteristic shadow in the retrograde pyelographic mediums. It is in this condition that cytologic urinary studies are often of great value. Not infrequently small pieces of tumor tissue may be passed in the urine which if recognized and examined will definitely establish the diagnosis. In others, sedimentation of the cells in the urine and fixation, mounting and staining may lead to the identification of villous fragments with epithelial cells characteristic of the papillary tumors of the pelvis.

Therapy and Prognosis.—Because pelvic tumors, especially of the papillary variety, are often associated with or followed by similar tumors in the lower part of the ureter, the operative procedure is complete ureteronephrectomy. The usual procedure is a flank or abdominal nephrectomy and the removal of the lower part of the ureter and the cuff of bladder by an extraperitoneal approach in the pelvis through the lower part of the abdomen. The immediate operative mortality of the combined operation is less than 2 per cent in some clinics.

With papillary tumors of the pelvis the prognosis is good. The metastases outside of the urinary tract occur late, and with an early removal this type of tumor gives the best prognosis of all renal tumors. If retroperitoneal metastases have occurred, as they may, though infrequently seen at the time of operation, the prognosis is bad because they are rather resistant to radiation. It seems the bleeding of these papillary tumors occurs early, and as a result these cases are not infrequently seen early. Occasionally a resection of the pelvis with the tumor as the center of the resected area may be necessary when the kidney is solitary; this has been followed without recurrence.

The squamous cell tumor of the pelvis and the undifferentiated carcinoma offer a poor prognosis. They both have invasive tendencies from the onset, may not present diagnosing symptoms for some time. At operation, extension of the tumor into the kidney itself and to the retroperitoneal nodes is usually found. It is in this latter type because of the exfoliation that studies in uterine cytology, like the vaginal fluid studies in uterine carcinoma, may offer an earlier diagnosis.

EMBRYOMAS OF CHILDHOOD (WILMS)

Embryonal carcinosarcoma, or Wilms' tumor of the kidney, is one of the more frequent carcinomas of childhood, an age in which cancer is rare but extremely malignant. It is a disease of infancy, the great majority of cases occurring before 2 years of age. More than 80 per cent of the reported cases occur before the seventh year. Rarely they may occur in adult life, and are then apparently less malignant. They are found in both sexes in about equal numbers and occur with about the same frequency in both kidneys. The tumors may be bilateral. They usually are not associated with external genitourinary malformations. It has often been reported that the children in whom these tumors occur are among the more comely children seen. Although occasionally trauma has been suggested as being associated with the tumor, there is no evidence or reason to believe that it plays any part in the production of the tumor.

These tumors may arise from any portion of the kidney. They may be in either pole or pelvic area and sometimes may be extrarenal. The tumors expand as they grow and may compress or surround the normal renal tissue. They are most frequently covered by the renal capsule, and grow rapidly with large round or lobular masses, most usually in the line of least resistance forward into the abdominal cavity. They may develop cysts within themselves and sometimes increase rapidly in size because of hemorrhage within the cysts. The microscopic picture is of embryonic renal elements with isolated tubules and glomeruli among the cancerous tissue, the appearance of giant cells and various epithelial cancer cells scattered among or co-existing with areas of sarcomatous tissue. Striated and nonstriated muscle cells may occur as well as other cancerous tissue structures.

These tumors are usually rapid growing. However, they apparently remain within the renal capsule for a considerable period, growing only locally and then later metastasizing. The metastases apparently are most often through the blood stream to the lungs and to the liver. Lymph metastases may occur to retroperitoneal and mediastinal nodes. Involvement of the skeletal system is not frequent. At times the tumor may grow directly through the capsule and involve adjacent organs. It is thought that metastases may be precipitated by rough handling of the tumor during examinations.

Symptoms.—There are no symptoms of Wilms' tumor in its early stage; no pain, no tenderness and usually no hematuria. The usual suspicion of its presence is when a mass is discovered in the abdomen or flank, or the size of the child's abdomen draws the attention of the mother or some other observer to the change. Hematuria is infrequent, occurring in less than 10 per cent of the

cases. Pallor, weakness and loss of weight may be present with or precede the finding of the abdominal mass, and they always are present late in the disease. Fever is not of infrequent occurrence and when present may be due to tumor necrosis

Fig. 4 (J.G.).—An intravenous pyelogram in a child with a large Wilms tumor of the right kidney. The left kidney is normal. The right shows a mass above which has displaced calyces laterally and obstructed them. The psoas line is obliterated on that side.

or to hemorrhage within the tumor. Urinary symptoms are usually absent; only occasionally may there be dysuria associated with the clots of the rare hematuria.

Diagnosis.—The diagnosis is made by noting a mass in an infant's loin or side of the abdomen. This mass is usually large, not tender, easily palpable, ballotable through the flank, rounded or lobular and the transverse colon may be anterior to the mass if it is the left kidney. The mass may or may not be fixed in the flank. If it feels lobular or cystic, the lobules cannot be transilluminated. Other conditions which may give a similar picture are conditions which are diagnosed by similar procedures. The various other conditions presenting a similar picture are carcinoma of the adrenal gland (sympathicoblastoma), chronic cystic fibrosis of the kidney, congenital obstructive hydronephrosis, congenital polycystic disease of the kidneys and the retroperitoneal sarcomas of childhood.

In all these conditions, including Wilms' tumor, urologic investigating procedures are absolutely necessary as soon as a mass is felt or suspected. Ordinary roentgenograms of the abdomen may show the mass in the flank and at times some calcification. As a rule little information is obtained from simple roentgenograms of the abdomen, and usually intravenous or subcutaneous secretory pyelograms are also done. If Wilms' tumor is present there is usually the normal secreting and anatomic kidney on one side and there may be diminished secretion on the affected side or calyceal or pelvic distortion as a contrast. At times the calyces may be displaced far from the pelvis. In large tumors there may be no or insufficient pyelographic mediums secreted by the kidney and cystoscopy with retrograde pyelograms may be needed to show the calyceal and pelvic distortion and loss of renal function, both due to tumor growth. Tumor cells may be found in the urine, but this is infrequent with Wilms' embryoma. The main roentgen observation is the shadows suggestive of changes in the renal parenchyma. These are entirely different from the normal but displaced pyelographic shadow seen with adrenal sympathicoblastoma, from the large reservoir of pelves and calyces seen with hydronephrosis, from the complete absence of pelvis or calyces and function with chronic cystic fibrosis, from the spidery bilateral changes with congenital polycystic disease and from the normal renal pyelographic shadow seen with retroperitoneal sarcoma.

Treatment and Prognosis.—The embryonal tumors of the kidney are among the most malignant of all renal growths. Their growth at times is extraordinary, and in a large number of cases death will occur in less than a year. In early recognition and in early therapy lies the hope for patients with these tumors. For a long time surgical treatment was considered to be hopeless in these cases, and high voltage roentgen therapy was considered to offer the better prognosis. At the same time and subsequently roentgen therapy was used to bring about a decrease in size of the tumor, to be followed by nephrectomy.

Due to the work of Ladd and his confreres,[4] at the Boston Children's Hospital a more serious study has been made of the removal of these tumors by the transperitoneal route with a minimum of handling either for diagnostic purposes or on the operating table, with ligation of the renal vessels and pedicle before displacement of the kidney and tumor. The result has been a much higher proportion of these cases free from recurrence than has formerly been reported. Similar reports have been issued from other clinics which show that better results may be obtained by earlier recognition of the tumor, avoidance of trauma by manipulation and earlier and more complete surgical treatment without trauma or dissemination of the tumor. According to reports at times complete disappearance of the tumor mass and freedom from recurrence follow high voltage roentgen therapy. Though this result is unusual, high voltage roentgen therapy is an essential therapeutic agent in cases in which pulmonary or other metastases demonstrated at time of diagnosis make surgical removal of the tumor unwise. The prognosis in these cases will be improved by the combination of early recognition of the condition and better surgical relief.

Wilms' tumors occur occasionally in adults, 53 cases having been collected from the literature by Esersky, Saffer, Panoff and Jacobi.[5] They have been reported in the seventh and ninth decades but are more frequent from 30 to 60 years. A mass in the abdomen is the usual symptom. The triad of hematuria, pain and mass is not always evident. Fever is frequent. The pyelographic studies show renal changes consisting in growth of a mass. Operative removal has been accomplished. Prognosis is poor even with postoperative radiation therapy, probably poorer than in infants.

(*To be Continued*)

4. Ladd, W. E., and White, R. R.: Embryoma (Wilms' Tumor), J. A. M. A. 127:1848, (Nov. 29) 1941.
5. Esersky, G. L.; Saffer, S. H.; Panoff, C. E., and Jacobi, M.: Wilms' Tumor on the Adult: Review of Literature and Report of Three Additional Cases, J. Urol. 58:397, 1947.

Clinical Notes, Suggestions and New Instruments

LIPOGRANULOMA OF THE PERITONEUM

Report of Three Cases Following the Intra-Abdominal Use of Liquid Petrolatum

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Many agents have been employed for the prevention of postoperative intra-abdominal adhesions. During the first two decades of this century, sterile oils were frequently introduced into the peritoneal cavity for this purpose. Their use in experimental animals led observers of this period to believe that such substances as wool fat, petrolatum and liquid petrolatum would inhibit the formation of adhesions.[1] These investigators, however, failed to allow sufficient time before sacrificing their animals, and this led to a false impression that sterile oils not only were harmless but would aid in the prevention of postoperative adhesions. It was later demonstrated that petrolatum and liquid petrolatum (Russian mineral oil) were intensely irritating to the peritoneum, were slowly absorbed, if at all, and resulted in the formation of granulomas and adhesions.[2] Norris and Davison, in 1934,[3] reported 2 patients, demonstrating the complications that follow the use of sterile liquid petrolatum in the abdominal cavity. The roentgenographic observations in most of these cases are characterized by calcareous deposits widely distributed throughout the peritoneal cavity, as seen in cases 1 and 2 reported here.

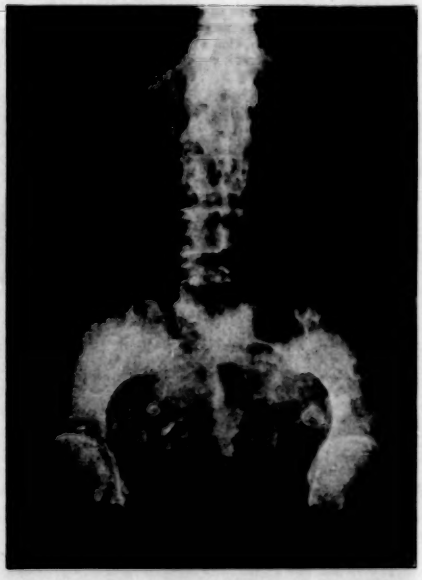

Fig. 1 (case 1).—Roentgenogram showing calcified lipogranuloma.

From the Whitehead Department of Surgery (Drs. Whitaker and Campelli) and the Department of Roentgenology (Dr. Walker), Emory University School of Medicine, and Grady Memorial Hospital.

1. Wilkie, D. P. E.: The Use of Oil in Abdominal Surgery, Surg., Gynec. & Obst. **10**: 126-132 (Feb.) 1910. Gellhorn, G.: Experimental Studies of Postoperative Peritoneal Adhesions, ibid. **8**: 505-513 (May) 1909. Blake, J. B.: The Use of Sterile Oil to Prevent Intraperitoneal Adhesions, ibid. **6**: 667-670 (June) 1908.

2. Cubbins, W. R., and Abt, J. A.: A Preliminary Report Concerning the Effect of Foreign Substances in the Peritoneal Cavity, Surg., Gynec. & Obst. **22**: 571-579 (May) 1916. Pope, S.: The Prevention of Peritoneal Adhesions by the Use of Citrate Solution, Ann. Surg. **63**: 205-207 (Feb.) 1916.

3. Norris, J. C., and Davison, T. C.: Peritoneal Reaction to Liquid Petrolatum, J. A. M. A. **103**: 1946-1947 (Dec. 15) 1934.

REPORT OF CASES

CASE 1.—Mrs. E. S., white, aged 65, was admitted to Grady Memorial Hospital May 23, 1947, complaining of cramping abdominal pain, vomiting and obstipation of two days' duration. A supracervical hysterectomy had been performed in 1924. Two years later the patient began to have frequent episodes of colicky abdominal pain due to partial intestinal obstruction. During the past twenty years she had been seen frequently in the outpatient department with similar complaints.

Fig. 2 (case 1).—Enlargement of roentgenogram showing calcified lipogranuloma.

Examination revealed moderate generalized distention and tenderness of the abdomen. Frequent peristaltic rushes were heard on auscultation, and an occasional visible peristaltic wave was observed. There was considerable induration in both vaginal fornices.

Roentgenographic examination of the abdomen showed numerous cystic calcific structures distributed throughout the abdomen, without significant arrangement in their distribution (figs. 1 and 2). Many of these structures were circular in contour; some had a mulberry-like appearance and others a serrated silhouette. They varied in diameter from 1 to 3 cm. The psoas and kidney shadows appeared normal. Several loops of distended small intestine were observed, suggesting the presence of obstruction.

A celiotomy was performed on the day of admission. The peritoneum was seen to be extremely thickened, and the entire peritoneal cavity was obliterated by dense adhesions. There were calcified nodules, varying in size from 0.5 to 3.5 cm., scattered throughout the peritoneal cavity. A loop of dilated small intestine was identified with difficulty, and a blind Witzel-type enterostomy was done. Histologic examination of several nodules showed dense fibrous tissue with metaplastic bone formation and calcification. A foreign body reaction was

represented in some areas by chronic inflammatory cells, large mononuclear phagocytes and foreign body giant cells surrounding large empty spaces. The cytoplasm of both the mononuclear phagocytes and the giant cells showed fairly large vacuoles (figs. 3 and 4). Histologic diagnosis was lipogranuloma.

Fig. 3.—Photomicrograph of biopsy specimen showing lipid vacuoles with surrounding foreign body reaction.

The patient slowly improved following operation and was discharged one month later.

Case 2.—Mrs. E. B., white, aged 53, was first admitted to Grady Memorial Hospital in 1924, at which time an inflammatory mass involving the right tube and ovary was excised. Sterile liquid petrolatum was placed in the peritoneal cavity. A laparotomy was performed five years later, and a tumor of the left ovary was removed. Examination nine years following the first operation revealed a firm mass that filled the entire pelvis. There were associated symptoms and physical observations consistent with partial obstruction of the small intestine. Dilated loops of small intestine were seen on roentgenographic examination. Multiple firm nodules were palpated through the anterior abdominal wall.

The patient was admitted to the hospital many times for recurrent intestinal obstruction, and eleven years following the first abdominal operation an exploration was performed because of persistent symptoms of intestinal obstruction. Dense multiple adhesions with "numerous metastatic plaques" on the intestinal serosa and paricta! peritoneum were observed. An ileostomy was performed. No specimen for biopsy was obtained. In December 1940, a celiotomy was performed because of symptoms of obstruction. A matted mass of peritoneal adhesions was encountered, and the exploration was abandoned after a specimen of a nodule was obtained for biopsy. Histologic examination revealed lipogranuloma of the peritoneum.

This patient was readmitted May 25, 1947, complaining of vomiting, abdominal distention and pain of three days' duration. There was slight abdominal distention; the peristalsis was hypoactive. She was moderately dehydrated. A roentgenogram of the abdomen at the time of admission revealed several loops of distended small intestine and a small amount of gas in the large intestine. Numerous calcareous ringlike densities (figs. 5 and 6), measuring up to 3 cm. in diameter, were seen throughout the abdomen; many were circular or oval in shape, but some had a mulberry-like appearance. These densities were most numerous along the inferior aspect of the diaphragm and in the region of the pelvic inlet. The psoas shadows and the lumbar part of the spine did not show significant pathologic changes.

Treatment was supportive, and a Miller-Abbott tube was passed. The patient became asymptomatic on the second hospital day and was discharged on the fourth day.

Case 3.—T. H., white, age 68, had liquid petrolatum introduced into his peritoneal cavity in 1927 following an appendectomy. Abdominal exploration was later carried out on two occasions (1928, 1934) for intestinal obstruction. He was admitted to Emory University Hospital Sept. 19, 1947, complaining of pain in the right upper quadrant of the abdomen and intolerance to fatty foods. Cholecystograms demonstrated a nonfunctioning gallbladder. Two large laminated opacities were seen in the right upper quadrant of the abdomen. On September 20, cholecystectomy was attempted, but was abandoned in the presence of a matted mass of leathery adhesions apparently distributed throughout the abdomen. Identification of abdominal viscera was impossible; the gallbladder was neither seen nor felt. Unfortunately, a biopsy specimen of the mass of adhesions was not obtained, but it is believed that the instillation of liquid petrolatum into the peritoneal cavity resulted in the symptoms and the operative observations in this case.

COMMENT

Following the introduction of liquid petrolatum into the peritoneal cavity, there occurs an intensive inflammatory reaction which results in the formation of dense adhesions between the viscera, mesentery and peritoneum.[4] This complication may require months or even years to develop fully. Late sequelae include widespread formation of grayish yellow nodules. Histologically, the nodules are cystic and are surrounded by fibrous

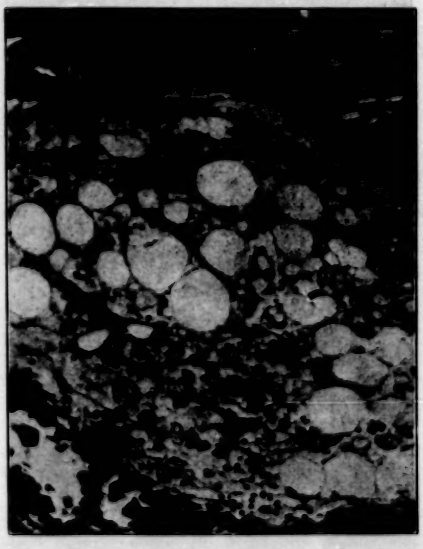

Fig. 4.—Photomicrograph of biopsy specimen showing lipid vacuoles with surrounding foreign body reaction. Calcification is shown in the dark area in the upper portion of the photomicrograph.

4. Cruickshank, A.: Paraffinoma of the Peritoneum, Lancet 1:4-6 (Jan. 4) 1941.

tissue which contains many foreign body giant cells. Most of the giant cells are located near large vacuoles which contain the liquid petrolatum. Calcification occurs late and is distributed at various points in the fibrous stroma, being most conspicuous in the periphery of the nodule.

The roentgenographic appearance of lipogranuloma of the peritoneum is characterized by multiple widely distributed calcareous cystlike structures throughout the peritoneal cavity. However, this roentgenographic pattern is not pathognomonic of this condition. Pugh [5] and Weig and his co-workers [6] described cases of pseudomyxoma peritonei in which similar calcareous deposits were seen roentgenographically and subsequently observed at operation. Pugh stated, however, that in one of his cases the possibility of paraffinoma could not be ruled out, since it was known that some foreign substance had been instilled into the abdomen at the time of a previous operation. Therefore, the differential diagnosis between pseudomyxoma and lipogranuloma can hardly be made on the basis of roentgenographic examination alone. Nevertheless, the recognition of the characteristic calcareous deposits is of great clinical importance, since it indicates in both conditions the presence of extensive peritoneal adhesions.

Calcareous structures in the abdominal cavity result from various factors which must be considered in the differential diagnosis of lipogranuloma. Calcified leiomyomas are usually few in number and possess a more flocculent type of calcification. Echinococcus cysts are limited in number and are more often located in the region of the liver. Usually a large parent

Fig. 5 (case 2).—Roentgenogram showing calcified lipogranuloma.

cyst is present. Opaque biliary and urinary calculi may be identified by proper roentgenographic procedures. Calcified lymph nodes rarely have a cystic appearance. Vascular calcifications are found in typical locations and are frequently tubular in character. Calcified appendices epiploicae may resemble lipogranulomas in individual lesions, but are fewer in number and are freely movable in the abdominal cavity.[7]

5. Pugh, D. G.: A Roentgenologic Aspect of Pseudomyxoma Peritonei, Radiology **39**: 320-322 (Sept.) 1942.
6. Weig, C. G.; Koenig, E. C., and Culver, G. J.: Pseudomyxoma Peritonei, Am. J. Roentgenol. **52**: 505-509 (Nov.) 1944.

SUMMARY

The cases reported here illustrate the intense inflammatory reaction in the peritoneum which may occur after the use of petrolatum and its derivatives in the abdominal cavity. The late development of recurrent obstructive symptoms was common in these cases. The roentgenographic observation of ovoid calcified bodies throughout the abdominal cavity is particularly significant. Similar roentgenographic observations may occur in pseudomyxoma peritonei. The history of a celiotomy performed during the period when the intraperitoneal use of oils was in vogue should lead one to suspect lipogranuloma peritonei. Tough dense adhesions throughout the abdominal cavity were observed in the 3 cases presented. Surgical intervention for obstructive symptoms in these cases is often hazardous and frequently futile.

Fig. 6 (case 2).—Enlargement of roentgenogram showing calcified lipogranuloma.

7. Morales, O.: Calcified Appendices Epiploicae as Freely Mobile Bodies in the Abdominal Cavity, Acta radiol. **25**: 653-661 (Nov. 21) 1944.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

The Council has authorized publication of the following statement.

AUSTIN SMITH, M.D., *Secretary.*

CORRECTION

Dr. James F. McCahey of Philadelphia has called attention to an inaccuracy in a former report of the Council on "Untoward Effects of Endocrine Therapy" (J. A. M. A. **125**:786-789, 1944) reading:

"In castrate and eunuchoid cases and in the male climacteric, testosterone provides a potent replacement therapy,[22]" with a footnote reference to Dr. J. B. Hamilton's article on testis therapy in "Glandular Physiology and Therapy." The reference number should have been placed directly after the words "castrate and eunuchoid cases," since the term "male climacteric" does not appear at any point in the article by Hamilton. The article was cited because of its warning against overstimulation by the use of testosterone replacement therapy.

The Council regrets that this error had escaped its attention. The question of the acceptability of testosterone in the treatment of the so-called male climacteric is being reconsidered by the Council in the light of further experience.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 2, 1948

WORLD MEDICAL ASSOCIATION

During the week of September 6-12, representatives of some thirty national medical associations met in Geneva to consider problems of current importance to the medical profession. Among the outstanding accomplishments was the elaboration of an inspirational pledge to be taken by young physicians throughout the world. The assembly considered also the development of a bulletin for the World Medical Association. This publication is to appear quarterly under the editorship of Dr. Morris Fishbein. A committee was also established to develop an international series of principles of medical ethics which would be acceptable to the national medical associations of all of the countries concerned. Among other questions given careful consideration was the establishment of suitable liaison with the World Health Organization of the United Nations and with UNESCO. The problems in which these groups may be jointly engaged would include the perfection of abstracting of the important medical literature of the world and the arrangement of international congresses in the field of medicine; also the place of the physician in time of war and the work now in process on the Pharmacopoeia. Significant also were discussions of the standardization of medical education on a high level throughout the world and plans for postgraduate medical education. Through the office of the secretary general, Dr. Louis H. Bauer, reports were made available on the status of the physician in various nations, on war crimes committed by German physicians and on many other subjects.

Most interest during the meeting centered on the adoption of a series of principles governing the provision of medical care under Social Security. Remarkable unanimity developed in the points of view of doctors throughout the world, all of whom were more concerned with the quality of medical service that could be rendered than with a widespread distribution of a low grade of medical care. THE JOURNAL will make available shortly the final text of the principles governing medical care under Social Security and also the final text of the pledge. These two documents constitute a landmark in medical progress, since they reaffirm the ethical ideals of the physician throughout the world and the common understanding of physicians everywhere as to the factors necessary for competent medical service.

DIETARY LIPIDS IN TUBERCULOSIS

About forty years ago Weigert [1] conducted feeding experiments with inoculated guinea pigs and concluded that the tuberculous process generalized more rapidly in animals fed a strict carbohydrate diet than in control animals receiving an additional liberal amount of milk fat. From this it seemed logical to assume that dietary lipids could produce only beneficial effects in tuberculosis.

Twenty years later this early assumption was challenged by Troteanu,[2] who administered cod liver oil directly into the stomach of guinea pigs previously inoculated intraperitoneally with bovine tubercle bacilli. The cod liver oil enhanced the progress of the experimental tuberculosis. This result was confirmed by Negre and his associates,[3] who found that the ingestion or subcutaneous injection of cod liver oil or olive oil resulted in an enhancement of experimental tuberculosis in both guinea pigs and rabbits. The opposite results were demonstrated with ethyl esters of palmitic, myristic, lauric, arachidic, capric and stearic acid. Given subcutaneously, these lipids retarded the appearance of experimental tuberculous lesions.

It seemed probable therefore that dietary lipids might exert either beneficial or deleterious effect in clinical cases, depending on the type of lipid used. This conclusion was tested by Dubos and Davis,[4] of the Rockefeller Institute, who studied the growth of Mycobacterium tuberculosis in liquid mediums containing a series of fatty acids. They found that capric, lauric, palmitic and myristic acids were inhibitory at dilutions as high as 1:10,000,000. Growth occurred at concentrations as high as 1:100 with stearic, oleic, linoleic or butyric acids.

Tests of the effects of feeding these antituberculous lipids are currently reported by Hedgecock,[5] of the department of bacteriology of St. Louis University. The lipids were administered to male Swiss albino mice 90 days of age in the form of oleic acid, olive oil, linseed oil or coconut oil. Each of the lipids was mixed with a fat-free, casein-supplemented ration in a concentration of 20 per cent. The four lipid-containing rations together with the nonlipid control ration were each administered to a group of 25 mice. After having

1. Weigert, R.: Berl. Klin. Wchnschr. **44**:1209, 1907.
2. Troteanu, V. C.: Compt. Rend. Soc. de Biol. **102**:141, 1929.
3. Negre, L.: Ann. Inst. Pasteur **49**:319, 1932. Negre, L.; Berthelot, A., and Bretey, L.: Ibid. **59**:457, 1937.
4. Dubos, R. J., and Davis, B. D.: J. Exper. Med. **83**:409, 1946.
5. Hedgecock, L. W.: Proc. Soc. Exper. Biol. & Med. **68**:106 (May) 1948.

been fed these rations for ten days, 5 mice of each group were set aside to serve as dietary controls. Five others were used for chemical analyses of body fat. The remaining 15 animals of each group were each inoculated intravenously with 0.5 mg. of recently isolated M. tuberculosis. The large dose was used because mice are known to be highly resistant to experimental tuberculosis.

Animals remaining alive at the end of thirty-seven days were killed with ether. Sections were prepared from the lungs, liver, spleen and kidneys of each animal at the end of the experimental period, and each organ was assayed for tuberculosis. The assay was based on the relative percentage of tissue of each organ involved. Thus: ± represented about 10 per cent coagulative necrosis, + represented 25 per cent necrosis, and so on to ++++, in which the pathologic involvement was about 95 per cent of the entire organ.

On this scale the least involvement (±) was recorded in the group fed coconut oil. With groups fed olive oil, oleic acid or linseed oil, many of the organs showed +++ involvement. Study of the weight loss showed that there was a smaller loss of weight and a lower mortality in the coconut oil group than with the group fed the other lipids.

Determinations of the saponification value and iodine value indicated that each dietary lipid was deposited in large amounts in the body fat. Chemical analyses also showed that coconut oil contains about 7 per cent capric, 46 per cent lauric, 19 per cent myristic and 10 per cent palmitic acid, the four acids found by Dubos to be particularly inhibitory to the in vitro growth of the tubercle bacillus.

The conclusion was drawn that 20 per cent addition of coconut oil to the routine casein-supplemented ration retards the progress of experimental tuberculosis in mice. An enhanced progress of tuberculosis is caused by the addition of similar amounts of olive oil, linseed oil or oleic acid. A direct application of these findings to clinical medicine, however, has not yet been suggested.

SALICYLATE THERAPY IN RHEUMATIC FEVER

To effect a cure of rheumatic fever, Coburn [1] claims, one of two objectives must be realized. Either the immune response of the host must be modified so that the patient recovers promptly after his first attack or the capacity of the infected micro-organism to elaborate antigen must be inhibited by a chemotherapeutic agent. Since neither of these objectives has yet been realized, one is limited to the suppression of the inflammatory reaction. If salicylate therapy can modify the sterile inflammatory reaction which occurs during activity of the rheumatic process, one might expect this effect to inhibit the development of cardiac disease.

Evaluation of any form of therapy in rheumatic fever, Coburn states, is difficult because about 20 per cent of young adults may be expected to have a monocytic attack and recover spontaneously under symptomatic treatment. About 40 per cent of 43 young adults treated with daily doses of 3 to 6 Gm. of sodium salicylate manifested rheumatic activity for more than one month and showed a definite tendency to contract valvular heart disease, while all of 18 patients treated with daily doses of 10 Gm. or more of sodium salicylate either orally or intravenously showed rapid clinical recovery and a progressive fall in the blood sedimentation rate. Although half of the 18 patients had electrocardiographic evidence of carditis on admission, in none did clinical signs of valvular heart disease develop.

By the method of determination of plasma salicylate concentration, developed by Brodie, Udenfriend and Coburn,[2] it was found that with the institution of daily oral doses of 10 Gm. of sodium salicylate the plasma level rose in forty-eight hours to between 331 and 454 micrograms per cubic centimeter, with an average maintenance level of 368 micrograms. At this plasma level the sedimentation rate of each patient fell within six days and continued to fall progressively to normal so long as this level was maintained. The induction of a high plasma salicylate level was followed not only by a rapid progressive fall in the blood sedimentation rate but also by a marked and rapid improvement in the clinical appearance.

Twenty patients maintained at 359 to 400 micrograms per cubic centimeter manifested a prompt and progressive subsidence of rheumatic inflammation, while 20 other patients with plasma levels below 250 micrograms per cubic centimeter continued to manifest an active inflammatory process. The intravenous administration of sodium salicylate is required to obtain a rapid rise in the plasma concentration of salicylate to 400 micrograms per cubic centimeter. In none of the 38 rheumatic patients treated with 10 Gm. of sodium salicylate daily did valvular heart disease develop, and in 21 out of 63 similar cases in which only small doses of sodium salicylate were given physical signs of heart disease developed. Coburn feels that a plasma salicylate level of at least 350 micrograms per cubic centimeter may be required to suppress the rheumatic reaction and that plasma level below 200 micrograms per cubic centimeter may be sufficient to relieve symptoms while masking a progressive inflammatory process.

Reid [3] treated patients having rheumatic fever with sodium salicylate orally and found that when the average plasma level concentration was less than 20 mg.

1. Coburn, A. F.: Salicylate Therapy in Rheumatic Fever, Bull. Johns Hopkins Hosp. 73: 435-464 (Dec.) 1943.

2. Brodie, B. B.; Udenfriend, S., and Coburn, A. F.: Determination of Salicylic Acid in Plasma, J. Pharmacol. & Exper. Therap. 80: 114-117 (Jan.) 1944.

3. Reid, J.: Does Sodium Salicylate Cure Rheumatic Fever? Quarterly J. Med. 17: 139-151 (April) 1948.

per hundred cubic centimeters the erythrocyte sedimentation rate showed no signs of falling; when the level was between 20 and 30 mg. per hundred cubic centimeters a slow fall was observed; when it was between 30 and 40 mg. the rate rapidly returned to normal. He argues that if the erythrocyte sedimentation rate can be accepted as a reliable index of rheumatic activity, then sodium salicylate has a curative action in the disease directly related to the plasma concentration of the drug. This conclusion is strongly supported by the observation that recurrence of the disease during oral treatment with salicylate coincides with pronounced fall in plasma salicylate level and subsequent remission with a secondary rise in the plasma level of the drug. It appears therefore that the main practical problem in the treatment of rheumatic fever is to know when enough salicylate is being given.

Reid concludes that effective treatment of rheumatic fever with salicylate demands that dosage should be controlled by repeated estimations of plasma or urinary salicylate. Cure of the disease depends not only on reaching but also on maintaining a high plasma salicylate level.

While salicylic acid is probably not the final solution to the therapeutic problems of rheumatic fever, with the development of blood level methods other drugs may be found to be more effective in suppressing the rheumatic reaction.

Current Comment

EMPLOYMENT OF THE HANDICAPPED

National Employ the Physically Handicapped Week beginning on October 3 has been set aside by President Truman to call attention to the courageous efforts of many disabled persons and to dramatize the activities of organizations engaged in rehabilitation. Repeated studies and demonstrations have shown that the physically handicapped employee is as dependable and productive as his normal co-worker and in many cases even more so. Reemployment would be more effectively accomplished if physicians understood the vital role that they must play throughout the entire rehabilitation procedure. Reassurance concerning reemployability will do much to prevent traumatic neurosis. Competent medical care of the disabled will aim to restore the injured to his former earning capacity in the same line of work and with minimum loss of time. When there is a residual disability that requires retraining and readjustment, the physician, the rehabilitation counselor and the work supervisor must work together in fitting job requirements to the physical ability. Work itself can be a potent therapeutic force. There is no greater contribution to peace of mind than congenial employment in safe and healthful surroundings. The National Committee in charge of Employ the Physically Handicapped Week bases its appeal to the public on terms of social and economic necessity. However, employment of the handicapped is not only good economy but also good medicine as well.

SILICOSIS

Silicosis continues to be a baffling problem after decades of study by professional and lay investigators. Patrick Heffernan, who has maintained an interest in this subject for many years,[1] comments[2] on the statement by Starling that "no substance introduced into protoplasm has any chemical influence on it unless it be soluble." Heffernan feels that the statement is misleading. As evidence, he refers to the "permutite" water softening process, a reaction between a solid and liquid, to the gas mask with the reaction between a solid and gas and, finally, to the more recent demonstration of the atomic architecture of minerals which show lattice structure. Comminution of minerals exposes fractured surfaces on which at numerous points free and unsatisfied valency forces exist whereby water can be attracted and held as water of constitution in the hydrated particle. Freshly powdered quartzite is just such a mineral, carrying powerful free and unsatisfied valency forces avid to take up water and other reactive material at its fractured surfaces. Obviously, when such powder comes in contact with protoplasm, it will hydrate itself at the expense of the fluid content of the protoplasm. The activity of mineral particles with other solids, liquids, or gases falls under four headings: (1) direct combination, (2) hydration, (3) oxidation and (4) hydrolysis. The behavior of dust produced from any rock formation can be estimated usually beforehand from its atomic lattice structure and depends on the existence at the fractured surfaces of free and unsatisfied valency forces. The fractured surfaces of a quartzite particle present a huge negative ion. A broken asbestos fiber can be active only at its fractured extremities, and a sheet of mica can be active, if at all, at its fractured edges only. As the particles become weathered, their activity disappears. Silica dust is more active chemically as a dry aerosol than in any wet vehicle. Heffernan says that the essential agent in the causation of true silicosis, as distinguished from nonspecific pneumonoconiosis, is the freshly cloven silica particle. The pathologic process basically consists of the hydration of the silica particle at the expense of the cell protoplasm. Because of its atomic lattice structures, quartzite, when powdered, yields a more virulent dust than other silica formations. Fully hydrated silica—silica hydrosol—sometimes mistakenly called "silicic acid," is nontoxic and enters freely into the metabolism of plants and animals, while partly hydrated suspension of silica in water, "colloidal silica," retains some of the chemical activity of the dry powder but in lesser degree. Thus we progress with the vastly important problem of silicosis. Exact knowledge of its cause will assure more successful control and preventive measures against this health hazard.

1. Heffernan, P.: Some Aspects of Silicosis, Tubercle **11**:481, 1930; J. Indust. Hyg. **8**:11, 1926; What Is Silicosis? Tubercle **16**:397, 1935.
2. Heffernan, P.: What Is Silicosis? Tubercle **29**:169, 1948.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Sept. 8, 1948.

Record in Physician-Attended Births

Data released by National Office of Vital Statistics show that 1946 marked a new high record in the matter of physician-attended births and births taking place in hospitals. Of the 3,288,672 live births recorded for the year, 2,708,223 (82.4 per cent) were in hospitals and 402,759 (12.2 per cent) were attended by physicians outside hospitals. Only 177,690 (5.4 per cent) were attended by midwives or other nonmembers of the medical profession. By contrast, in 1935 only 37 per cent of confinements were in hospitals, slightly more than one half were attended by physicians outside hospitals and in 1 out of 8 midwives or other nonprofessional persons were utilized.

The statistical picture reveals significant differences between white and nonwhite groups and between urban and rural areas. All but 1.6 per cent of the white births were attended by physicians, and 87.1 per cent occurred in hospitals. For nonwhite births, the physician in attendance percentage was 65.2, and only 45.2 per cent took place in hospitals. For city residents, 97.9 per cent had physicians and 92.5 per cent of the births were in hospitals. Corresponding percentages for rural dwellers were 89.6 and 67.1.

Orthopedic Surgeons on New Certification Board

Drs. H. H. Kessler, Atha Thomas and R. H. Alldredge are the three physician members of the first board of directors of the American Board for Certification of the Prosthetic and Orthopedic Appliance Industry. The other four members of the board, all of whom are laymen engaged in the artificial limb industry, are Chester C. Haddan, Denver; David E. Stolpe, New York; Lee J. Fawver, Kansas City, and J. B. Korrady, Chicago. Announcement of the board's election and of Mr. Haddan's election as its president was made in Washington by Glenn E. Jackson, secretary of the committee which arranged for establishment and incorporation of the new American Board. Its function will be to set up standards for certification of qualified limb fitters and of the firms by which they are employed. Approximately 400 of the estimated 575 manufacturers of prosthetic and orthopedic appliances in the United States participated in the mail ballot poll which resulted in approval of the certification plan and election of the four lay members of the directors' board, said Mr. Jackson. The three medical members were unopposed.

Progress in Aviation Medicine

Objectives and accomplishments of the aeromedical and aviation psychologic research programs currently being conducted under technical supervision of the Air Surgeon are described briefly in the U. S. Air Force annual report made public August 22. The 112 page illustrated report cites: development of a flying suit that will enable aircrewmen to perform their duties with safety and in comfort at 60,000 feet; progress toward perfection of an internally ventilated flying suit that will give the wearer a "temperature tolerance" ranging from minus 60 F. to plus 180 F.; rising emphasis on development of lighter and readily transportable surgical and medical equipment.

"A preliminary proposal for an air-borne hospital utilizing the most recent equipment has been prepared that promises to revolutionize medical field operations in support of air-borne operations," says the report.

"To further medical progress and to meet urgent civilian emergency needs, the Air Force has made much of its specialized equipment available to research institutions and physicians. A number of low-pressure chambers with accessories, for example, have been loaned to American universities, and during the infantile paralysis epidemic of last year Air Force resuscitation apparatus, and even aircraft for emergency evacuation, were utilized for civilian care."

Progress Report on Bone Strength Study

The National Bureau of Standards has published a technical report on the progress of investigations which it is conducting, with cooperation of the Naval Medical Research Institute, on mechanical properties of human bones. Initiation of the research was prompted by military necessity to acquire information which might prove useful in protecting aviation personnel in crashes, seat ejection from aircraft and in parachute openings. Another practical military consideration is the injury frequently caused to sailors when the ship's deck buckles as the result of an explosion, fracture of the os calcis being a common occurrence in such instances.

Initial work in the cooperative study involved seventeen tests on specimens made from compact type bone from extremities of human beings and monkeys. Of the fourteen specimens tested in compression, with the direction of the load parallel to the fibers of the bone, it was demonstrated that their average ultimate strength was about 23,000 pounds per square inch. "These preliminary data," said the report, "indicate that bone may be considered an elastic, brittle material, having about one fourth the compressive strength of cast iron and more than twice that of hickory wood."

"Model" Milk Ordinance

Thirty-four million Americans are now protected through a model milk ordinance whose nationwide adoption was recommended by the U. S. Public Health Service. The estimate was made in conjunction with issuance by the U. S. Public Health Service of a compilation of disease outbreaks in 1946 which were ascribed to milk and milk products. During that year, according to reports forwarded to Washington by state and territorial health authorities, there were twelve such outbreaks. Eleven involved raw milk and the other followed accidental contamination of pasteurized milk by a toxic chemical. There were six other outbreaks in which milk was suspected but not conclusively incriminated. The milk ordinance is now effective in 1,207 municipalities and 207 counties in 39 states. It has been incorporated into state regulations in 31 states, 2 of which enforce compulsory pasteurization.

Navy Reports on Incidence of Phlebitis and Sinusitis

The Navy Department's Bureau of Medicine and Surgery has completed ten year studies on the incidence of phlebitis and sinusitis. Regarding the former, compiled data show that 6,222 cases were reported among Navy and Marine Corps personnel between 1936 and 1945, inclusive, in addition to which there were 1,131 readmissions. The peak was reached in 1945, when 63 out of each 100,000 persons in uniform were on the sick list with phlebitis. During the same decade, sinusitis cases totaled 39,553 for an average incidence rate of 357.5 per 100,000. It was estimated that one eighth of the cases existed prior to entry into military service. The peak year was 1943 (464.4 per 100,000) but beginning in 1944 and continuing to the present rate has declined steadily.

Dr. Robert J. Anderson Heads Public Health Service Tuberculosis Division

Dr. Scheele, Surgeon General of the U. S. Public Health Service, has appointed Dr. Robert J. Anderson as medical director and chief of the Tuberculosis Division. He succeeds Dr. Francis J. Weber, who has been assigned to postgraduate work in psychiatry at Johns Hopkins University. Dr. Anderson formerly was assistant chief of the division.

Information Center on Child Life Research

A new office that will function as a clearing house of information on medical and other types of research relating to children's health and welfare has been set up in the Children's Bureau, Federal Security Agency. Clara E. Councell has been appointed director of the unit, which will be under the general supervision of Dr. Martha M. Eliot, associate chief of the Bureau.

GOVERNMENT SERVICES

ARMY

COORDINATE QUARANTINE REGULATIONS

Public health quarantine regulations of the Canal Zone and the United States have been coordinated in a way that will facilitate maritime and air commerce after September 1. As of this date, ships and aircraft receiving complete public health quarantine clearance at a port in one of these areas will not be required to undergo quarantine inspection on arrival at the other area, unless stops are made at a foreign country en route.

Surgeon General Leonard A. Scheele of the U. S. Public Health Service explained that quarantine inspections are performed primarily to prevent importation of the internationally designated "quarantinable diseases": cholera, transmitted by infected food or water or by contact; plague, transmitted by the rat flea or contact; typhus, transmitted by lice; smallpox, transmitted by contact, and yellow fever, transmitted by the Aedes aegypti and other mosquitoes. Ships are inspected before being permitted to dock unless specifically exempted. A sanitary inspection is made, and the ship fumigated if a rat colony is found on board. Air travelers are inspected in a quarantine room at the airport before being permitted to come in contact with persons at the place of arrival. During flight from yellow fever areas airplanes are sprayed on the inside to kill mosquitoes, and they may be sprayed again on arrival.

Health officials have declared that under the provisions of revised quarantine regulations the new United States-Canal Zone procedure for exempting ship and aircraft from inspection will be entirely safe with respect to disease control.

THE HOTTEST PLACE IN NORTH AMERICA

A study prepared for presentation to the American Meteorological Society by Arnold Court, meteorologist in the Office of the Quartermaster General in Washington, shows that the hottest place on the North American continent is the surface of the ground in Death Valley in Southeastern California during the month of July. On the basis of averages covering a period of thirty-six years, a maximum temperature of 180 F. may be expected on the desert floor on one day every seven years, while at 5 feet above the ground, where official temperatures are recorded, the reading would be 125 F. Weather observations in Death Valley were begun April 30, 1891, when a temporary weather bureau station was set up on Furnace Creek. In June 1911, a cooperative station of the Weather Bureau was established at Greenland Ranch, 178 feet below sea level, where observations have been taken by the foreman of the Pacific Coast Borax Company once each day ever since, with few exceptions. The highest temperature ever reported for Death Valley, 5 feet above the ground, was on July 10, 1913, when 134 F. was registered; during the week of July 7-14, 1913, the maximum for each day did not fall below 127 F., a record which has not since been equaled. July temperatures show wide spreads between maximum and minimum, and the minimum reported for Greenland Ranch was 68.26 F. in 1938.

THE STERNBERG EXHIBIT

The sixth exhibit in the series, "Famous Men of Army Medicine," currently presented by the Army Medical Museum, is devoted to George Miller Sternberg, Surgeon General of the Army from 1893 to 1902, who, during his distinguished career, was a president of the American Medical Association and of many other scientific societies. Dr. Sternberg is said to have seen more service on the battlefield during the Civil War than any other medical officer. After this period he acquired wide experience in dealing with cholera and yellow fever epidemics, and this led him to take up the study of bacteriology on which much of his fame rests. He was the first in this country to show the organisms of tuberculosis, malaria and cholera, and the first to teach American physicians the fundamental principles and technics of bacteriology. Among many other accomplishments, he was the author of a textbook on bacteriology.

MEDICAL MEETING IN KOREA

On August 11, the Army medical officers stationed in Korea met at the 34th General Hospital and were addressed by Dr. Lenox K. Baker of Duke University College of Medicine, Durham, N. C., who is touring the command as a consultant in orthopedic surgery. Dr. Baker lectured on "Low Back Pain" and made ward rounds. At the afternoon session, Lieut. Col. John J. Marren, commanding officer of the hospital, presided; Dr. Baker discussed Colles' and Pott's fractures; Lieut. Morton Goldman discussed hepatic function tests, and Lieut. Rolf Andreassen presented a case report; Lieut. Duane presented a paper entitled "Fractures and Dislocations of the Spine," which was discussed by Dr. Baker. A picnic supper was held in the evening at the officers' club.

EXTEND TRAINING PROGRAM LIMIT

The Surgeon General's Office announces that the date on which applications may be received from young doctors to take advantage of the Army's graduate training program has been extended to November 1. Under the program, selected medical graduates may serve their internships and residencies in civilian hospitals of their own choice, with first lieutenant's pay, but at the end of their year's training interns must apply for regular Army commissions and may apply for residency training; residents may continue their residency toward specialty qualification. Each, however, is required to serve a year of active duty for each year of training at Army expense.

PERSONAL

The British Ambassador to the United States, Sir Oliver Franks, presented decorations at the British Embassy in July to Dr. John F. Fulton and Brigadier General Edgar E. Hume, both of whom are honorary consultants for the Army Medical Library.

MISCELLANEOUS

COURSES IN RADIOISOTOPES

The Oak Ridge Institute of Nuclear Studies announces that four additional radioisotope courses have been scheduled as follows: October 25 with industrial personnel having priority; Jan. 3, 1949, government personnel; Feb. 14, 1949, medical personnel, and March 14, 1949, general. Thirty-two participants will be accepted in each course, and the four weeks' period will be divided into laboratory work, lectures on laboratory experiments, general background lectures and special topic seminars. Information may be obtained from Dr. Ralph T. Overman, Special Training Division, P. O. Box 117, Oak Ridge, Tenn.

NATIONAL SECURITY RESOURCES BOARD

The following chiefs of sections of the Medical Division of the National Security Resources Board have been appointed, thus virtually completing the staff of the Medical Division: Rear Admiral Thomas Carlyle Anderson, M.C., U. S. N., in charge of the unit dealing with medical and related man power; Lieutenant Colonel Howard B. Nelson, in charge of planning for health supplies; Vincent B. Lamoureux, in charge of sanitary engineering aspects of national security, and Ruth Freeman, in charge of the division's section on public health nursing.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Arkansas

Hutchinson, James H. Jr.....Monticello
Ledbetter, John P.....Jonesboro
May, J. T.....Little Rock

California

Brinkerhoff, Elmer E.....Oakland
Chole, Arthur S.....Los Angeles
Durand, Robert L.....Colfax
Lake, Thomas L.....Berkeley
Marchildon, John W.....Hollywood
Matthews, Ephraim D.....Kerman
Pinkerton, Allan L.....Los Angeles

Connecticut

Hickey, Joseph P.....Hartford
Martin, John S.....Naugatuck

District of Columbia

Marbury, William B. Jr.....Washington

Florida

Edwards, Harry M.....Gainesville
Merlin, Hyman.....Miami
Morgan, John M.....Sanford

Idaho

Mackey, Oliver M. Jr.....Lewiston

Illinois

Condon, Joseph V.....Chicago
Hogan, Charles C.....Peoria
Kagen, Irving N.....Chicago
Mueller, Ferdinand J.....Belleville
O'Connor, Edward F.....Chicago
Roland, Samuel I.....Chicago
Sperlino, Harry.....Chicago
Trapanese, Dominic R.....Forest Park
Weyl, Wolfgang L.....Chicago

Indiana

Chivington, Paul V. Jr.....Indianapolis
Fortner, Joseph G.....Vincennes
Harrington, James F. Jr.....Richmond
Martz, Bill L.....Anderson
Ramsdell, Glen A.....La Porte

Iowa

Corton, Richard V. M.....Waterloo

Kentucky

Clarke, William F.....Prestonsburg

Louisiana

Avant, James A. Jr.....New Orleans
Baffes, Thomas G.....New Orleans
Fontenelle, Irwin L.....New Orleans

Maryland

Bennett, Eben T.....Baltimore
Holbrook, William A. Jr. College Park
Pratt, Louis J. Jr.....Baltimore
Straham, Charles.....Baltimore

Massachusetts

Street, Russell B. Jr.....Conway

Michigan

Blothouse, Robert E.....Muskegon
Caughey, Andrew F. Jr.....Ann Arbor
Domnitch, George O.....Detroit
Picard, Joseph D.....Dearborn
Schmitt, Phillip E.....Howell
Van Ommen, Ray A.....Zeeland
Venier, Anton G.....Detroit
Zawacki, Sigmund G.....Dearborn

Minnesota

Borgen, Alfred E.....Culver
Danielson, Charles D.....Minneapolis
Glaeser, John H.....Swansville

Minnesota—Continued

Lie, Dagfinn.....Fisher
Stimac, Emil M.....Virginia

Mississippi

Gee, Happy L.....Sumner
Martin, Raymond S. Jr.....Jackson

Missouri

Eder, Gerald J.....Clayton

Nebraska

Lutt, Carl J.....Omaha
Morgenstern, Nathan L.....Omaha

New Hampshire

Duprey, William G. Jr...North Conway

New Jersey

Belle, Louis J.....Elizabeth
Feuerstein, Sidney S. West New York

New York

Deaugustinis, August S.....New York
Fish, Gilbert D. Jr.....Palham
Hall, Robert A.....Albany
Hull, John G.....Tupper Lake
Johnson, Angelo G.....Hunter
McManus, Richard G..... New Rochelle
Mark, Herbert.....New York
Morse, William R.....Niagara Falls
Murphy, James S.....New York
Shapiro, Lawrence.....Brooklyn

North Dakota

Johnson, Paul L.....Taylor
Kulland, Roy E.....Palermo
Olmstead, Edwin G.....Enderlin
Paulson, Wallace J.....Grand Forks

Ohio

Bohl, Robert W.....Hillsboro
Buhrman, Charles M.....New Carlisle
Centa, Charles J.....Cleveland
Coburn, Donald J.....University Heights
Dyer, Robert D.....Worthington
Fecher, Mark P.....Dayton
Hanna, James L.....Cleveland
Hesselbrock, John J.....Cincinnati
Kasle, Travis.....Toledo
Klumph, Thorp A. Jr.....Canton
Marks, Bernard H.....Columbus
Peirce, Robert J.....Cincinnati
Resch, Frederick A.....Youngstown
Saylor, Mark L.....Canal Winchester
Shively, Frank L. Jr.....Dayton
Stechschulte, Jerome B..Columbus Grove
Woodcock, Charles W.....Warren

Oklahoma

Bradshaw, John O.....Welch
Burgtorf, Richard H.....Custer City

Oregon

Heckhard, Roy E.....Seaside
Lymann, Howard W.....Portland

Pennsylvania

Bedrossian, Edward H.....Drexel Hill
Benjamin, Craig L.....Wayne
Conwell, Quentin R.....Philadelphia
Cutler, Irvin.....Philadelphia
Crosley, Archer P. Jr.....Wyncote
DeLozier, Joseph W.....Hollidaysburg
Drinker, Henry M.....Jenkinstown
Fisher, Harry.....Munhall
Greenberg, Marvin S.....Philadelphia
Guerin, Paul F.....Erie
Hayes, James C.....Pittsburgh
Hughes, George V. G.....Pittsburgh

Pennsylvania—Continued

Kilduff, Charles J. Jr.....Coatesville
Kresock, Joseph W.....Carbondale
Liddell, Joseph S.....Pittsburgh
Loftus, Joseph A.....Hudson
Lovette, John B.....Spangler
Madonna, Harry M.....Philadelphia
Manno, Bruno V.....Scranton
Masucci, Elmo F.....Scranton
Podkul, Theodore B.....Wilkes-Barre
Sugarman, Leroy A. South Coatesville
Sweetser, Arthur A. Jr.....Scranton
Wiest, Hiram L.....East Petersburg

Rhode Island

Leonard, William A. Jr.....Providence
Sherer, Joseph F. Jr.....Little Compton
Turco, Vincent J.....Westerly

Texas

Barth, John H.....Yoakum
Brown, George W.....Jacksonville
Culver, George A.....Corpus Christi
Duff, Bedford K.....Galveston
Duff, Robert L.....Galveston
Dumas, Lawrence W. Jr.....Dallas
Durham, Charles A.....Houston
Gilliland, Robert M.....Galveston
Gary, Charles L. Jr.....Dallas
Henry, Marshall G.....Dallas
Holmes, James E.....San Antonio
Mims, Arthur T.....Dallas
Moore, William L. Jr.....Austin
Obenchain, Thomas H. Jr.....Dallas
Purnell, James E.....Austin
Rudnick, Leon R.....Mabank
Scheurich, Richard E.....Goose Creek
Sparks, Tom C. Jr.....Amarillo
Spiller, William F. III.....Houston
Spivey, Dan.....Lufkin

Utah

Lamb, Harold B. .....Salt Lake City

Virginia

Bell, Cecil C. Jr.....Lynchburg
Levitt, Herbert M.....Petersburg
Shiuh, E. Ling.....Richmond

Washington

Berg, Arthur W.....Cathlamet
Lindstrom, Toivo A.....Auburn
Mooney, James G.....Roslyn

West Virginia

Robinett, Paul W.....Huntington

Wisconsin

Dockery, Joseph N.....So. Milwaukee
Duguid, Robert H.....Sparta
Green, Ray E.....Fond du Lac
Hoff, Allen D.....Viroqua
Kennedy, James A.....Oshkosh
Otto, Owen.....Madison
Shearer, Charles E.....Edgerton
Wheeler, Clayton E. Jr.....Viroqua

Wyoming

Hanna, Joe T.....Lingle

Canal Zone

Clark, Sidney B.....Balboa Hghts

Puerto Rico

Maestre, Federico J.....Utuado

Canada

Horsley, George E.....Vancouver
Kert, Morley J.....Ottawa
McLauchlan, Duncan A.....Chemainus

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as rebate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CONNECTICUT

Personal.—More than forty doctors of Meriden, Wallingford and Southington joined the Meriden Medical Society, June 16, in paying honor to Dr. Fessendon N. Otis, Meriden, on the occasion of his retirement June 30 from the Meriden Hospital, where for many years he was head of the radiology department. Dr. Otis received an inscribed sterling silver tray showing testimonials of high regard expressed at the meeting.

Postgraduate Education at Yale.—First formal courses of postgraduate education for Connecticut physicians began the last week in September with a course in gastroenterology. The program is sponsored jointly by Yale University and the Connecticut State Medical Society under the direction of Dr. William R. Willard, Assistant Dean of Yale (THE JOURNAL April 17, p. 1055). Twelve sessions of two hours each will be devoted to diseases of the gastrointestinal tract and interrelationships with diseases of other organs. This course runs through December 16. An orientation course for part time physician anesthetists will be offered in eight all-day sessions October 11 to November 30. Laboratory and clinical demonstrations and discussions will be conducted from October 13 to December 1. A review of present knowledge and new developments in endocrinology will be given on Wednesdays from 6:30 to 10 p. m., and ten sessions in obstetrical practice will be given between October 5 and December 7. A course in surgical diagnosis will run from September 29 through December 15. Other courses will include orthopedics, demonstrations in anatomy, cardiovascular disease, metabolism, nutrition and diet, infectious diseases, pathology and early diagnosis of cancer.

FLORIDA

Medical Supplement in Newspaper.—The Escambia County Medical Society sponsored an eighteen page medical supplement in the regular Sunday edition of the *Pensacola News-Journal* June 27. A committee from the medical society assembled and edited copy submitted by doctors, nurses, health officials, welfare agencies and others. The cooperation and support of business firms in Pensacola helped make the enterprise possible. Comment on the medical supplement indicates that the reception by the public was favorable. The project was a revival of a successful venture of prewar days.

ILLINOIS

Record Low Infant Mortality.—The Illinois Department of Public Health reports fewer than 18 stillbirths per thousand live births during the first quarter of 1948, an all time low. Record low mortality rates were also recorded for babies under 1 month and for babies under 1 year, 19.2 and 28.9, respectively, per thousand live births. Neonatal mortality was higher among residents of the Southern Region (21 per thousand live births). Lowest neonatal rate was among residents of the Peoria Metropolitan Area, 14 per thousand live births. The death rate for premature births for the entire state is 9.5 for every thousand live births. The highest rate, 10.1 per thousand, was found in the Chicago Metropolitan Area. The maternal death rate for the state, 1.1 per thousand, was exceeded in the Central Area where 1.7 mothers per thousand live births died, and mortality among mothers of newborn babies in the Central Area was over four times as heavy as for mothers in the Northern Area.

Chicago

Public Lecture Series on Tuberculosis.—The Tuberculosis Institute of Chicago and Cook County is presenting a series of seven free lectures on tuberculosis at the Museum of Science and Industry on Sunday afternoons at 3 p. m. The remaining lectures, all by Chicago physicians, will be:

Oct. 3, Drs. Robert G. Block, Edwin R. Levine and Henry C. Sweany, Round Table Discussion, Treatment of Tuberculosis.
Oct. 10, J. Edmond Bryant, The Slums and Tuberculosis.
Oct. 17, William F. Petersen, Tuberculosis and the Climate.
Oct. 24, George C. Turner and Dr. Levine, Round Table Discussion, Can Vaccination Control Tuberculosis?
Oct. 31, Arthur W. Newitt, Tuberculosis Control in Chicago.

Study Recommendations of Health Survey.—Plans for a drive to put into effect the recommendations of the Chicago-Cook County Health Survey completed last year will be the duty of a committee being formed under sponsorship of the Health Division of the Council of Social Agencies of Chicago. Chairman of the committee is Samuel A. Goldsmith, director of the Jewish Charities. The division is now determining the number of recommendations of the survey that have already been adopted by the governmental and other agencies of the county. When this study is completed, expansion and financing of health departments will be outlined for an intensive campaign throughout the county. The Chicago-Cook County Health Survey was made by the U. S. Public Health Service, at the request of Edward J. Kelly, then mayor, and Clayton F. Smith, then president of the county board. They acted at the suggestion of a committee representing the Council of Social Agencies, the Chicago Medical Society and the Institute of Medicine of Chicago. The reports, forty-one in all, evaluated health facilities of the community and made detailed and practical recommendations for improvement. Major emphasis in the coming campaign is expected to be placed on the expansion of the Chicago Health Department and the Cook County Department of Public Health.

INDIANA

Personal.—Dr. Carl H. McCasky, chairman of the executive committee of the Indiana State Medical Association, presented a paper on "Surgery of the Laryngeal Disease" September 7 before the Pan-Pacific Surgical Association at Honolulu, Hawaii. The association is composed of all countries bordering on the Pacific Ocean.

University News.—Surgical research has been added to the program of the Indiana University School of Medicine, Bloomington-Indianapolis, with the appointment of Dr. Leslie W. Freeman as director of surgical research and the granting of a fellowship in surgery to Dr. Joseph C. Finneran. The program will be under the supervision of Dr. Harris B. Shumacker Jr., professor and chairman of the department of surgery. Dr. Freeman, previously associated with Dr. Shumacker in a similar capacity at Yale University, New Haven, Conn., served as chief of paraplegia services at Vaughan Hospital, Hines, Ill., and at Kennedy General Hospital, Memphis, Tenn., when it was taken over by the Veterans Administration. Dr. Finneran, a graduate of Harvard University, Cambridge, Mass., and Johns Hopkins University School of Medicine, Baltimore, recently completed an internship in surgery at Johns Hopkins Hospital.

MAINE

Research Program of Jackson Memorial Laboratory.—The new plan for organization of the work of the Roscoe B. Jackson Memorial Laboratory appears as part of the annual report released August 27. The first section deals with the laboratory's research program, a twelve month activity, whose objective is to use genetic methods and material as a basis for research in biology and medicine with special emphasis on the growth and development of mammals. This is under the direction of George W. Woolley, Ph.D., the laboratory's assistant director. A supply service to 150 major research laboratories constitutes the second phase of the program. The scientific supervision of this work is under Elizabeth S. Russell, Ph.D., at the main units of the laboratory. Year around cooperation will be maintained with practical breeders of small mammals. The Summer Research Center for Visiting Investigators involves ten weeks or more of activity. This phase of the program affords opportunity for visiting investigators to use special material and technics available at the laboratory. A second objective is to bring into contact with the resident staff for the exchange of ideas, persons with new and varied points of view and skills. The Training School for Scientific and Medical Students will include year round opportunities for certain students, aside from its ten weeks of intensive summer activity, including those who will work for the doctorate under cooperative agreement with established universities. The trustees have decided to exclude from the Jackson Laboratories all of the radioactive isotopes and all animals and materials exposed to them, but a controlled population of mice will be constantly maintained at the laboratory for staff members wishing to take material to other laboratories for work with isotopes.

MARYLAND

County Society Program.—The Montgomery County Medical Society, meeting on the third Tuesday of each month at the Manor Country Club, Norbeck, has arranged the following programs for the rest of 1948:

October 19, A. Magruder MacDonald, Washington, D. C., The Duties and Functions of the Coroner's Office.
November 16, Brian B. Blades, Washington, D. C., Tumors of the Chest.
December 21, Frank P. Foster, Boston, Diseases of the Thyroid Gland.

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MASSACHUSETTS

Dean Burwell Resigns.—Dr. C. Sidney Burwell, dean of Harvard Medical School, Boston, since 1935, has resigned effective Feb. 1, 1949. He will continue actively as research professor of clinical medicine in the medical school and at the Peter Bent Brigham Hospital. Dr. Burwell received his M.D. degree from the Harvard Medical School in 1919. After World War I he spent some time as a member of the American Red Cross Commission in Western Russia. He came to Harvard from Vanderbilt University School of Medicine, Nashville, Tenn., where he had been professor of medicine and physician in chief at the Vanderbilt University Hospital. Earlier he taught and performed research at Harvard and at the John Hopkins Medical School.

Appoint Professor of Psychiatry.—Dr. William Malamud, clinical professor of psychiatry, has been appointed chief of the Boston University School of Medicine's department of psychiatry and psychology, and full time professor of psychiatry, also consultant in psychiatry on the staff of Massachusetts Memorial Hospital and chief of psychiatric service of the outpatient department. Dr. Malamud has been a part time member of the Boston University faculty for eight years and head of the department of psychiatry since 1946. He is chairman of the training committee of the U. S. Public Health Service, Division of Mental Hygiene; chairman of the Committee on Mental Education of the Group for the Advancement of Psychiatry, and counselor of the American Psychological Association. A graduate of McGill University Faculty of Medicine, Montreal, Canada, 1921, Dr. Malamud was associate professor and professor of psychiatry at the University of Iowa from 1929 to 1939. Since then he has served as clinical professor of psychiatry at Boston University School of Medicine and Tufts College Medical School.

MICHIGAN

Gordon Scott Appointed Acting Dean at Wayne University.—Gordon H. Scott, Ph.D., chairman of the department of anatomy at Wayne University College of Medicine, Detroit, has been named acting dean of the college to fill the vacancy left by the resignation of Dr. Hardy A. Kemp (THE JOURNAL, August 14, p. 1474). Dr. Scott joined the Wayne University staff in January 1945, having held a similar chairmanship at the University of Southern California School of Medicine, Los Angeles. He had previously served at the Rockefeller Institute for Medical Research in New York and the Washington University School of Medicine in St. Louis. During World War II he handled work in connection with the government's Office of Scientific Research and Development. He did graduate work at Johns Hopkins University and the University of Minnesota.

Symposium on Protoplasm.—The Detroit Institute of Cancer Research will present a symposium on the Fundamental Properties of Protoplasm October 4-6 on the occasion of the dedication of its laboratories. The scientific session will be held in the Horace H. Rackham Educational Memorial Building. Physicians included on the extensive program are:

Carl F. Cori, St. Louis, Recent Work with Crystalline Enzymes.
Harry S. N. Greene, New Haven, Conn., Biological Assessment of Tissue Potentialities.
F. Peyton Rous, New York, The Natural History of a Cancer.
Charles S. Cameron, New York, The Professional Education Program of the American Cancer Society.
Murry M. Copeland, Washington, D. C., Benign Lesions of the Breast.
Willard M. Allen, St. Louis, Clinical Uses of the Sex Hormones.
Stuart W. Harrington, Rochester, Minn., Malignant Lesions of the Breast.
Douglas Quick, New York, Cancer of the Head and Neck.
Bradley L. Coley, New York, Diagnosis and Treatment of Bone Tumors.
Thomas E. Jones, Cleveland, Carcinoma of the Rectum and Sigmoid.

The clinical program has been arranged by the Cancer Committee of the Wayne County Medical Society and is sponsored by the Education Committee of the American Cancer Society, Southeastern Michigan Division.

NEBRASKA

Form Nebraska Medical Foundation.—The Nebraska Medical Foundation, Inc., was formed recently through the efforts of the Nebraska State Medical Association. The purpose of the foundation is to carry on an effective medical education program in the medical sciences, to further research through providing facilities and training for personnel and, in general, to improve medicine and medical care in Nebraska. Through the work and intensive efforts of Dr. Harold S. Morgan, Lincoln, and his committee, which was authorized in 1948 by the council of the state association, the foundation became a reality.

NEW YORK

Erie County Society Meeting.—The Medical Society of the County of Erie will begin its fall programs with its second Clinical Afternoon and Evening, October 20 at the Hotel Statler, Buffalo. Speakers will be:

George E. Slotkin, Buffalo, Results of the Treatment of Urinary Tract Tuberculosis with Streptomycin and Chaulmoogra Oil.
Geza de Takats, Chicago, Treatment of Cerebral Apoplexy.
Charles D. Marple, New York, Use of Anticoagulants in Thromboembolic Conditions with Particular Reference to Coronary Thrombosis and Myocardial Infarction.
Jere W. Lord Jr., New York, Surgical Treatment of Portal Hypertension.

A subscription dinner in honor of the guest speakers will be served between afternoon and evening sessions. Tickets at $5 each may be secured from the county society in Buffalo.

New York City

University Appointment.—Dr. William L. Watson, of the thoracic surgical service staff of Memorial Hospital for the Treatment of Cancer and Allied Diseases, was appointed associate professor of surgery at the New York University College of Medicine, August 1.

Bronx Society of Neurology and Psychiatry.—The Bronx Society of Neurology and Psychiatry has recently been incorporated with thirty-six members. Its officers are: Dr. Joshua H. Leiner, president; Dr. Jacob H. Friedman, secretary, and Dr. Moses J. Madonick, treasurer.

Emotional Aspects of Rehabilitation.—Joseph Levi, Ph.D., formerly chief clinical psychologist, Veterans Administration Hospital, Bronx, has been appointed research psychologist at the Institute of Rehabilitation, New York University-Bellevue Medical Center. He will be a member of a psychiatric team studying the emotional aspects of rehabilitation under a $73,500 grant from the Commonwealth Fund to New York University College of Medicine.

Venereal Disease Campaign.—The City of New York Department of Health, with the cooperation of the New York State Department of Health and the U. S. Public Health Service, will launch a month's campaign November 8 to bring under treatment an estimated 250,000 hidden cases of venereal diseases in the city. Representatives of the medical profession have assured the health department of their cooperation, and leaders in the fields of education, religion, health and welfare have been consulted in planning the campaign. Columbia University has prepared a series of fifteen radio transcriptions for broadcast during the campaign.

NORTH CAROLINA

Symposium on Therapy.—Duke University School of Medicine, Durham, will present a Symposium on Therapy November 4-6, at the school of medicine and Duke Hospital. Speakers include:

Harry Gold, New York, Newer Trends in the Management of Congestive Failure.
Carl V. Moore, St. Louis, Recent Advances in the Treatment of Anemia.
Harry L. Rogers, Philadelphia, Recent Therapeutic Trends in Allergic Diseases.
Cornelius P. Rhoads, New York, Recent Advances in the Treatment of Malignant Neoplastic Disease.
William L. Bradford, Rochester, N. Y., Recent Development in the Prevention and Treatment of Certain Communicable Diseases.
Wallace E. Herrell, Rochester, Minn., Present Status of Antibiotic Therapy.
Stewart H. Clifford, Boston, The Prevention of Neonatal Mortality.
Carl F. Schmidt, Philadelphia, Newer Trends and Methods in the Development of Therapeutic Agents.
Willard O. Thompson, Chicago, Therapeutic Advances in Endocrinology.
Richard H. Freyberg, New York, Treatment of Rheumatism and Allied Disorders.
Joseph E. Moore, Baltimore, Treatment of Syphilis.
Willis J. Potts, Chicago, Special Surgical Problems of Children.

On Friday at 8 o'clock a round table discussion and questions and answers program will be conducted with Dr. O. H. Perry Pepper, Philadelphia, as a moderator.

OHIO

Personals.—Dr. F. William Sunderman has been appointed head of the department of clinical pathology at the Cleveland Clinic Foundation. Dr. Sunderman received his M.D. and Ph.D. from the University of Pennsylvania, Philadelphia. During the war he was medical director of the Explosives Research Laboratory and an investigator and consultant for a division of the Office of Scientific Research and Development.——Dr. Shelby G. Gamble, assistant professor of physical medicine, Ohio State University College of Medicine, Columbus, has been appointed head of the department of physical medicine at the Cleveland Clinic, Cleveland. He has held similar position at the Starling-Loving University and Children's hospitals in Columbus.

Pediatric Psychiatry.—A new program of training in pediatric psychiatry is in progress at the University of Cincinnati College of Medicine, under the direction of Dr. Richard E. Wolf, assistant professor of pediatric psychiatry. The program is financed by the Commonwealth Fund and the Cincinnati Children's Hospital. Dr. Wolf serves in a consultant capacity for physicians at the Children's Hospital, working along with the physicians on their cases. He holds weekly conferences with hospital nurses and house staff and, in the fall, will lecture to students in the medical college. He is a graduate of Harvard University, Cambridge, Mass., and the University of Pennsylvania School of Medicine, Philadelphia. He has been on the university faculty since 1943.

OKLAHOMA

Spastic Paralysis Treatment Center.—Oklahoma's first center for the treatment of spastic paralysis was recently opened on the South Campus at the University of Oklahoma School of Medicine, Oklahoma City. The Norman Spastic Paralysis Institute is licensed for a maximum of 25 patients.

Postgraduate Study.—Hillcrest Memorial Hospital, Tulsa, will present its second Postgraduate Study Course, fall session, September 7 to December 30 for interns, residents and practicing physicians. There is no fee for the lectures, which are held every evening except Saturday and Sunday from 6 to 7 o'clock.

Personal.—Dr. Arthur A. Hellbaum, professor of physiology, University of Oklahoma School of Medicine, has been named associate dean of graduate studies and research.——Harold A. Shoemaker, Ph.D., has resigned as assistant dean, a position that he held since 1939, but will continue as professor of pharmacology.——Dr. Patric H. Mayginnes, Tulsa, has retired after fifty-one years' practice, forty of which have been in Tulsa. ——The council of the Oklahoma State Medical Association has announced the appointment of Mr. John K. Hart as associate executive secretary of the association.

WASHINGTON

Seattle Mass Chest Survey.—Seattle is the fourth city in the nation and the first on the West Coast to inaugurate a mass chest roentgenogram survey. Surveys in Washington, Minneapolis and St. Paul have been completed. The program is sponsored by the Seattle-King County Health Department, the King County Anti-Tuberculosis League and the King County Medical Society. The state department of health, which is furnishing two mobile x-ray units, and the U. S. Public Health Service, which is furnishing sixteen mobile x-ray units, are cooperating with the sponsoring agencies.

Dr. Bennett to Head Anatomy Department.—Dr. H. Stanley Bennett, assistant professor of cytology, department of biology, Massachusetts Institute of Technology, Cambridge, has been appointed professor of anatomy and executive officer of the department of anatomy at the University of Washington School of Medicine, Seattle. Dr. Bennett obtained his M.D. degree from Harvard Medical School Boston, 1936. After an internship at Johns Hopkins Hospital, he was a fellow of the National Research Council and research fellow in anatomy. From 1939 to 1944 he was instructor in anatomy and pharmacology at Harvard Medical School, where he was made associate in anatomy in 1941. From 1942 until 1946 he served in the U. S. Navy.

WEST VIRGINIA

Health Conference Meeting Date Changed.—The annual meeting of the Northern District Health Conference, originally scheduled for October 8 at Fairmont, has been changed to October 22 to enable health workers to attend the psychiatric seminar at Huntington, October 6-7.

Cerebral Palsy Clinic.—A clinic for children with cerebral palsy was formally opened September 25 at Charleston under the sponsorship of the Kanawha County Society for Crippled Children and Adults. The clinic, which will be held in the Kanawha-Charleston Health Department clinic rooms, will be open from 9 to 4 every other Saturday, but it is expected that arrangements can be made soon to hold the clinic at least once each week. Treatment at the present time will be limited to 10 children, but every effort will be made to expand facilities so that additional patients may be accommodated. An orthopedist, a pediatrician, a physical therapist, an occupational therapist and a speech therapist will be in attendance at each session of the clinic, which will be in charge of the members of the medical advisory board. The West Virginia Department of Public Assistance, the Kanawha County Board of Education, the Parents Council (parents of cerebral palsied children), the American Business Club, Alpha Chi Omega, and other interested groups are working actively with the Crippled Children's Society in formulating plans for the clinic.

GENERAL

Meeting of International Cancer Research Commission Postponed.—The meeting of the International Cancer Research Commission, which was to have been held in Paris October 17-22, has been postponed until next year.

Medical Record Librarians Meeting.—The American Association of Medical Record Librarians will meet at the Elks Club, Los Angeles, October 18-22. Included in the program are three panel discussions: Standard Nomenclature on Monday evening, Statistical Data of Hospital Reports on Wednesday afternoon and a Medical-Legal Panel Friday morning. Sectional meetings will be held Friday afternoon.

Meeting of Clinical Pathologists.—The American Society of Clinical Pathologists will hold its annual meeting at the Drake Hotel, Chicago, October 12-15. The scientific program will open with a symposium on the cytologic diagnosis of cancer, followed by other scientific papers and the presentation of the Ward Burdick Award to Dr. Paul R. Cannon, Chicago. Scientific exhibits will be included. The annual banquet will take place October 13 at 7:30 p. m.

National Society Meeting.—The annual convention of the National Society for Crippled Children and Adults, Inc., will be held at the La Salle Hotel, Chicago, November 15-17. Outstanding speakers in the fields of medicine, health and education will discuss progress in work with the handicapped during the past year. The convention will be attended by physicians, therapists, educators, workers with the handicapped and representatives of the society's more than 2,000 state and local units throughout the United States, Canada, Alaska and Hawaii.

Millions for Cancer Research.—The American Cancer Society has awarded $3,500,000 for cancer research in the year beginning September 1. Specific allotments include Columbia University, $242,288 in fellowships and individual and institutional grants; Memorial Hospital and the Sloan-Kettering Institute, $136,276, and Cornell University, $76,205. The largest allotment was made to the University of Chicago, which will receive $332,047. Institutions and individual scientists in thirty states participate in the awards, with groups in New York state receiving about one sixth of the total. Massachusetts, Illinois and Pennsylvania follow in that order.

Meeting of the Society for Study of Arteriosclerosis.—The American Society for the Study of Arteriosclerosis will hold its annual meeting at the Hotel Knickerbocker, Chicago, October 31 to November 1 under the presidency of Dr. William B. Kountz, St. Louis, Mo. Papers to be presented include the following:

I. Mark Scheinker, Cincinnati, Cerebral Vascular Changes in Arterial Hypertension.
Konrad E. Bloch, Ph.D., Chicago, Some Aspects of the Intermediary Metabolism of Cholesterol.
William H. Davis, Two Harbors, Minn., Clinical Diagnosis of Arteriosclerosis.
Russell L. Holman, New Orleans, Studies on the Relationship of Diet and Renal Insufficiency to Arterial Disease.
Rudolf Altschul, Saskatoon, Canada, New Experiments in Arteriosclerosis.

The guest speaker at the banquet October 31 at 7:30 p. m. will be Dr. Cassius J. Van Slyke, Washington, D. C., director, National Heart Institute.

Marriages

WILLIAM CARL LUDWIG DIEFENBACH III, Long Island, N. Y., to Miss Martha Kahle of Shelter Island, September 11.

HOWARD CARTER DAVIS JR., Greenwich, Conn., to Miss Patricia Nichols French of New York, July 20.

CHARLES R. WILLSON, Wilmington, Ill., to Mrs. Sallie Satterfield of Nokomis at Taylorville, July 2.

RICHARD E. H. DUISBERG, Philadelphia, to Miss Agnes Adamy of New Brunswick, N. J., July 16.

DAVID L. ROSENCRANS, Towanda, Pa., to Miss Barbara S. Allen in Montclair, N. J., July 17.

MARLIN BOYD HOGE to Miss Martha Nell Greenwood, both of Little Rock, Ark., August 16.

CHARLES M. ALLABEN, Binghamton, N. Y., to Mrs. Mary K. Stevens in Buffalo, July 1.

WILLIAM R. DEWAR to Miss Thelma J. Neidig, both of Allentown, Pa., July 10.

HELMUT BAUM, Berlin, Germany, to Miss Betty Marsh of St. Paul, August 22.

PHILIP H. BAKER to Miss Judith Elster, both of Los Angeles, July 11.

Deaths

Solomon Solis-Cohen, Melrose Park, Pa., died in the Jewish Hospital, Philadelphia, July 12, aged 90, of bronchopneumonia and parkinsonism. Dr. Solis-Cohen was born in Philadelphia Sept. 1, 1857 and received his medical degree from Jefferson Medical College, Philadelphia, in 1883. Five years later he was appointed lecturer in clinical medicine. He was professor of clinical medicine from 1902 to 1927, when he was made emeritus professor. Dr. Solis-Cohen had been professor of clinical medicine and therapeutics at the Philadelphia Polyclinic and the College for Graduates in Medicine from 1887 to 1902 and lecturer in therapeutics at Dartmouth College from 1890 to 1892. In 1902 and 1903 he was chairman of the Section on Materia Medica, Pharmacology and Therapeutics of the American Medical Association and in 1907 a member of the House of Delegates. He was a fellow of the College of Physicians of Philadelphia, American College of Physicians and the American Association for the Advancement of Science and an honorary member of the Medical and Chirurgical Faculty of Maryland and other medical societies. From 1899 to 1913 he was a recorder for the Association of American Physicians, and in 1898 and 1899 was president of the Philadelphia County Medical Society. Dr. Solis-Cohen served on the Philadelphia Board of Education from 1925 to 1944 and on the council of the Jewish Agency for Palestine from 1920 to 1942, and he was a founder of the Jewish Theological Seminary of America. From 1887 to 1927 he was physician at Philadelphia General, Jefferson and Jewish hospitals and later was consulting physician. He was a trustee of the United States Pharmacopoeia from 1920 to 1940, and was the author of "Therapeutics of Tuberculosis," 1891, "Essentials of Diagnosis" with A. A. Eshner, 1892-1900, and "Pharmacotherapeutics, Materia Medica and Drug Action" with T. S. Githens, 1928, and editor and contributing author of "A System of Physiological Therapeutics" in eleven volumes, from 1901 to 1904. In 1899 he was a delegate to the third Zionist Congress in Basle.

Berthold Steinbach Pollak ● Jersey City, N. J.; born in Vienna, June 26, 1873; Dartmouth Medical School, Hanover, N. H., 1896; member of the House of Delegates of the American Medical Association in 1928 and from 1931 to 1933; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served as vice president and president of the Hudson County Medical Society; member and director of the National Tuberculosis Association, which he represented at various times as delegate at conferences of the International Union Against Tuberculosis at London, Paris, Lausanne, Brussels, Oslo, Warsaw and Washington; named U. S. delegate to a tuberculosis conference held in Rome; member and director of the American Heart Association and the American Trudeau Society; past president of the New Jersey Public Health and Sanitary Association, New Jersey Tuberculosis League and the New Jersey Hospital Association; member of the executive committee of the Hudson County Tuberculosis League; chairman of the medical board of the Deborah Jewish Consumptive Sanatorium in Browns Mills; phthisiologist at St. Mary's Hospital, Hoboken, Beth Israel Hospital, Newark, Jersey City Medical Center and Christ Hospital; early in his career appointed medical director of the Hudson County Tuberculosis Hospital, which in 1946 was renamed in his honor the Berthold Steinbach Pollak Hospital for Chest Diseases; died in his apartment at the hospital June 27, aged 75, of cerebral thrombosis.

Otto Marburg, New York; born in Roemerstadt, Austria, May 25, 1874; Medizinische Fakultät der Universität, Wien, Austria, 1899; clinical professor of neurology at the Columbia University College of Physicians and Surgeons; member of the American Medical Association and the New York Academy of Medicine; honorary member of the American Neurological Association, the Philadelphia and New York Neurological societies, the Vienna Medical Society and various other scientific associations; served as a vice president of the International Neurological Congress; specialist certified by the American Board of Psychiatry and Neurology; for many years chief of the Neurological Institute of the University of Vienna; on the consulting staffs of Montefiore Hospital and the New York Post Graduate Medical School and Hospital; author of "Microscopic Topographic Atlas of the Central Nervous System," the third edition published in 1927, and many other books on his speciality; died in the Mount Sinai Hospital June 13, aged 74.

Otho August Piedler ● Sheboygan, Wis.; born in Stockbridge, Wis., March 9, 1873; Wisconsin College of Physicians and Surgeons, Milwaukee, 1902; past president of the state board of health, State Medical Society of Wisconsin and the Sheboygan County Medical Society; served in the Spanish-American War and with the American Expeditionary Forces in France during World War I; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine; formerly assistant professor of surgery at the Marquette University School of Medicine, Milwaukee; past president and formerly chief of staff of the Sheboygan Clinic, of which he had been one of the organizers in 1921; instrumental in the organization of the Sheboygan Memorial Hospital, where he had been chief of staff and where he died June 22, aged 75, of coronary thrombosis and carcinoma of the bladder.

David von den Berg Le Mone ● Columbia, Mo.; born in Grand Rapids, Mich., July 21, 1904; Washington University School of Medicine, St. Louis, 1934; associate professor of roentgenology at the University of Missouri School of Medicine; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; chief of staff of Boone County Hospital; roentgenologist at Audrain Hospital, Mexico, St. Joseph's Hospital in Boonville and St. Mary's Hospital in Jefferson City; roentgenologist at the University Hospitals and the Ellis Fischel State Cancer Hospital; consulting roentgenologist at the State Hospital in Fulton and the Missouri State Penitentiary Hospital in Jefferson City; died in Glockner Hospital, Colorado Springs, June 11, aged 43 of coronary thrombosis.

Thomas Trovillo Sheppard ● Pittsburgh; born in Pittsburgh, Sept. 17, 1891; Columbia University College of Physicians and Surgeons, New York, 1918; associate professor of medicine at the University of Pittsburgh School of Medicine; president of the Allegheny County Medical Society; past president of the Pittsburgh Academy of Medicine; on the staffs of the Magee, Presbyterian and Eye, Ear, Nose and Throat hospitals; director of the Renziehausen Memorial Ward and Clinic at Children's Hospital; member and chief of staff at Western Pennsylvania Hospital, where he died July 5, aged 56, of encephalomalacia and arteriosclerosis.

Harry Anthony Keenan, Stoughton, Wis.; Rush Medical College, Chicago, 1903; served during World War I; lieutenant colonel, medical reserve corps, not on active duty; past president of the board of trustees of the Lake View Sanatorium in Madison; on the visiting staffs of the Methodist Hospital in Madison and Stoughton Community Hospital; member of the American Medical Association; in 1943 was selected by *Look* magazine as the typical home front physician in wartime; died in the Wisconsin General Hospital, Madison, July 1, aged 70, of cerebral thrombosis and diabetes mellitus.

James Edwards Poore ● Lieutenant Colonel, U. S. Army, retired, Washington, D. C.; born on Feb. 24, 1876; Bellevue Hospital Medical College, New York, 1897; veteran of the Spanish-American War; served on the Mexican border in 1916 and overseas during World War I; served with the Army of Occupation in Germany; postwar duties included service in China and the Philippines; entered the medical corps of the U. S. Army as a major in 1920; promoted to lieutenant colonel in 1937; retired Feb. 29, 1940; died in the Walter Reed General Hospital April 3, aged 72.

John Wesley Judd ● Ithaca, N. Y.; born in 1870; University of Vermont College of Medicine, Burlington, 1896; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; fellow of the American College of Surgeons; past president of the Tompkins County Medical Society; served as health officer and coroner; affiliated with Tioga County General Hospital in Waverly and on the staff of Tompkins County Memorial Hospital, where he was president of the staff and where he died June 6, aged 78, of heart disease.

Sarkis H. Abkarian, Pelham, N. Y.; University of the City of New York Medical Department, New York, 1889; died in the New Rochelle (N. Y.) Hospital June 24, aged 85, of cerebral thrombosis and arteriosclerosis.

Frank Benjamin Allison, Detroit; Detroit College of Medicine, 1905; member of the American Medical Association; affiliated with St. Luke's Hospital; died in the Harper Hospital June 30, aged 68, of coronary thrombosis.

Harry William Vernette Beals ● Mayview, Pa.; Temple University School of Medicine, Philadelphia, 1937; interned at the Hamot Hospital in Erie; member of the American Medical Association; served in the medical corps, Army of the United States, during World War II; associated with the Mayview Hospital; died June 26, aged 37, of coronary occlusion.

Richard Lorenzo Brown, Gloster, Miss.; Cincinnati College of Medicine and Surgery, 1889; member of the American Medical Association; died in McComb, June 18, aged 81.

William J. Burns, Glen Cove, N. Y.; Bellevue Hospital Medical College, New York, 1882; at one time health officer of the town of Oyster Bay; died in May, aged 89.

Edward Buehler Clement ● Salisbury, N. C.; Jefferson Medical College of Philadelphia, 1906; served during World War I; died in Brunswick, Ga., June 18, aged 66, of coronary occlusion.

William Henry Chambers, Dierks, Ark. (licensed in Arkansas in 1903); died in Little Rock June 4, aged 69.

Corbon Jay Decker ● Surgeon, Lieutenant Commander, U. S. Navy, retired, Athens, Ga.; Jefferson Medical College of Philadelphia, 1880; entered the U. S. Navy in July 1906 and retired Aug. 31, 1907 for disability resulting from an incident of service; served during World War I; died in the General Hospital June 21, aged 86, of coronary thrombosis.

Walter den Bleyker ● Kalamazoo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; city physician in Kalamazoo from 1906 to 1908; past president of the Kalamazoo Academy of Medicine; at one time superintendent of Fairmount Hospital; died June 29, aged 71, of heart failure.

Frederick Luke Doucett, Weymouth, Mass.; Tufts College Medical School, Boston, 1900; member of the American Medical Association; for many years a member and formerly chairman of the board of health; died June 19, aged 78, of arteriosclerotic heart disease and cerebral hemorrhage.

Harry Baker Dow, West Springfield, Mass.; Baltimore Medical College, 1911; also a pharmacist; member of the board of health; died in the Springfield (Mass.) Hospital June 7, aged 71, of hypertensive cardiovascular disease and hemiplegia.

Stanley Waldo Dowling ● Santa Cruz, Calif.; Cooper Medical College, San Francisco, 1912; died in the French Hospital June 26, aged 60, of carcinoma of the colon and coronary thrombosis.

Henry Cuttino Dozier, Ocala, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; member of the American Medical Association and the Southeastern Surgical Congress; fellow of the American College of Surgeons; past president of the Florida Medical Association; on the staff of Monroe Memorial Hospital; died in Lavallette, June 16, aged 69, of coronary occlusion.

Henry A. Dunphy ● Palmer, Mass.; Baltimore Medical College, 1908; associate medical examiner for the Palmer district of Hampden County; served on the staff of Mercy Hospital in Springfield, where he died June 11, aged 66, of cerebral embolism.

Willis E. Elder, Columbus, Ohio; College of Physicians and Surgeons, Baltimore, 1895; formerly assistant chief medical examiner of the Ohio State Industrial Commission; died June 14, aged 81, of chronic myocarditis.

Carrie Innes Felch, Boston; Tufts College Medical School, Boston, 1906; member of the American Medical Association; died June 11, aged 75, of cerebral hemorrhage.

Elisha Flagg, Boston; Harvard Medical School, Boston, 1901; member of the American Medical Association; at one time treasurer of the Boston Medical Library; served on the staff of Massachusetts General Hospital; died June 8, aged 82, of heart disease.

W. Sturgis Frankenburger ● Carmichaels, Pa.; Jefferson Medical College of Philadelphia, 1911; served during World War I; formerly member of the school board; died June 1, aged 61, of coronary occlusion, arteriosclerosis and diabetes mellitus.

Henry Gray Glover, Jackson, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1882; member of the American Medical Association; died June 21, aged 87, of coronary thrombosis.

James Minos Godfrey, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1904; Jefferson Medical College of Philadelphia, 1906; professor emeritus of anesthesia at the Hahnemann Medical College and Hospital of Philadelphia; member of the American Society of Anesthesiologists; died at Buck Hill Falls, Pa., June 30, aged 67, of carcinoma of the left lung.

Charles Augustus Goodrich ● Hartford, Conn.; Columbia University College of Physicians and Surgeons, New York, 1896; member of the New England Pediatric Society; past president of the Hartford County Medical Society; affiliated with Hartford Hospital, where he died June 13, aged 76.

Herschel Willman Goss, Indianapolis; Indiana University School of Medicine, Indianapolis, 1929; member of the American Medical Association; died May 21, aged 44, of cerebral hemorrhage and malignant hypertension.

William Brandon Gregory ● Owego, N. Y.; Syracuse University College of Medicine, 1934; interned at the Binghamton City (N.Y.) Hospital; died in Lima, Ohio, June 12, aged 41, of injuries received in a plane crash.

Bert C. Hall, Pompeii, Mich.; Detroit College of Medicine, 1897; fellow of the American College of Surgeons; for many years associated with the R. B. Smith Memorial Hospital in Alma; died June 30, aged 80, of coronary embolus.

F. L. C. Helm ● Baltimore; Georgia College of Eclectic Medicine and Surgery, 1912; formerly coroner of the Western District; on the staff of the Church Home and Hospital; died in Bon Secours Hospital June 7, aged 64, of thyrotoxicosis.

William Francis Hill, Jersey City, N. J.; Columbia University College of Physicians and Surgeons, New York, 1919; died in the Jersey City Medical Center June 20, aged 52.

Wilgus Alexander Holman, London, Ohio; Jefferson Medical College of Philadelphia, 1923; member of the American Medical Association; died June 10, aged 50, of coronary occlusion.

Vincent Joshua Horton ● Calmar, Iowa; State University of Iowa College of Medicine, Iowa City, 1923; died in the Kahler Hospital, Rochester, Minn., May 31, aged 51, of embolism following an operation.

Edward Lamar Kelly, Repton, Ala.; Medical College of Alabama, Mobile, 1900; for many years county health officer; member of the American Medical Association; died June 5, aged 77, of cerebral hemorrhage.

John Timothy Kennedy ● Medical Inspector, Commander, U. S. Navy, retired, Ogunquit, Me.; University of the City of New York Medical Department, New York, 1894; fellow of the American College of Surgeons; entered the U. S. Navy in 1900 and retired June 30, 1936; died in Naval Hospital, Portsmouth, June 3, aged 75, of coronary thrombosis.

Perry Firestone King ● Alliance, Ohio; Western Reserve University Medical Department, Cleveland, 1904; fellow of the American College of Surgeons; affiliated with Alliance City Hospital; for many years closely identified with Mount Union College; died May 16, aged 70, of coronary occlusion.

Edgar Thorp Lassetter, Albuquerque, N. M.; Southern College of Medicine and Surgery, Atlanta, 1913; also a graduate in pharmacy; veteran of the Spanish-American War; a member of the state board of health and the board of trustees of the Lovelace Foundation for Medical Education and Research; vice president of the board of governors of the Lovelace Clinic; on the staff of St. Joseph Hospital; died June 27, aged 73, of cerebral hemorrhage.

Carl Copeland MacCorison ● North Berwick, Me.; Dartmouth Medical School, Hanover, N. H., 1906; for many years superintendent of the North Reading (Mass.) State Hospital; died in the Henrietta D. Goodall Hospital, Sanford, June 3, aged 70.

John Harry Mallery, Trail, Ore.; Medical Department of the University of California, San Francisco, 1902; served during World War I; formerly affiliated with the U. S. Public Health Service reserve and on the staffs of various Veterans Administration hospitals; died June 30, aged 70, of heart disease.

Earle Clarence McBride ● Terre Haute, Ind.; University of Louisville Medical Department, 1907; served as president of the Terre Haute Academy of Medicine and the city board of health; chief of medical service of St. Anthony's Hospital; died June 5, aged 73, of coronary occlusion.

Vincent Valens McCabe, Millbrook, N. Y.; Baltimore Medical College, 1901; died May 30, aged 73, of subdiaphragmatic abscess and toxemia.

Leo Thomas McCready, Boston; Tufts College Medical School, Boston, 1906; member of the American Medical Association; examining physician for the local Selective Service Board during World War II; died May 5, aged 68, of carcinoma of the larynx.

Edel Farnandis McIntosh Sr., Chattanooga, Tenn.; Meharry Medical College, Nashville, 1912; formerly city physician; died May 8, aged 60, of coronary occlusion.

John Franklin Mecluskey ● Philadelphia; Maryland Medical College, Baltimore, 1911; on the staffs of the Episcopal and St. Mary's hospitals; died in the State Hospital, Marlboro, N. J., June 9, aged 71, of cerebral hemorrhage.

Henry Chalmers Mitchell, New Castle, Pa.; Jefferson Medical College of Philadelphia, 1903; member of the American Medical Association; medical examiner for the public schools; on the staff of the Jameson Memorial Hospital, where he died June 6, aged 69, of carcinoma of the liver.

Edward Everett Moore, Mount Airy, N. C.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; died in Morganton May 26, aged 89.

John Aloysius Murphy, New Haven, Conn.; New York University Medical College, New York, 1897; on the staff of the Hospital of St. Raphael, where he died June 1, aged 76, of carcinoma of the transverse colon.

James Cheston Ogden ● Long Beach, Calif.; State University of Iowa College of Medicine, Iowa City, 1930; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of Seaside Memorial, St. Mary's and Community hospitals; died May 25, aged 45.

Thomas L. Peacock, Lake Odessa, Mich.; Michigan College of Medicine and Surgery, Detroit, 1899; died May 27, aged 79, of valvular heart disease.

Clarence Fay Rinkle, New Hartford, N. Y.; Albany (N. Y.) Medical College, 1916; died May 30, aged 60, of pulmonary tuberculosis.

Gus Thompson Rumbaugh, Villisca, Iowa; Kentucky School of Medicine, Louisville, 1890; died in Clarinda May 1, aged 81, following a fracture of the right hip due to a fall.

George Walter Sapp, Newark, Ohio; Ohio State University College of Medicine, Columbus, 1911; member of the American Medical Association; died May 23, aged 61, of coronary occlusion.

Henry Snure ● Los Angeles; University of Louisville School of Medicine, 1910; specialist certified by the American Board of Radiology, Inc.; fellow of the American College of Physicians; member of the American Roentgen Ray Society, Radiological Society of North America and the American College of Radiology; served during World War I; for many years on the staff of California Hospital; died in St. Vincent's Hospital May 17, aged 60, of cerebral hemorrhage.

George Elmer Strout ● Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; formerly assistant professor of ophthalmology and otolaryngology at his alma mater; chief of staff, Wells Memorial Dispensary; member of the staffs of University, Eitel, Northwestern and St. Barnabas hospitals; oculist to the Minneapolis and St. Louis Railroad; died May 10, aged 75, of coronary thrombosis and myocardial infarction.

Martillus L. Todd ● Major, U. S. Army, retired, Charleston, S. C.; Baltimore Medical College, 1897; at one time on the faculty of his alma mater; entered the medical corps of the U. S. Army as a major in 1920 and retired Jan. 31, 1931 for disability in line of duty; served during World War I; died in the Roper Hospital, May 30, aged 78, of carcinoma of the prostate.

LIEUT. HILERD W. JENKINS
(MC) U.S.N.R., 1914-1942

COMDR. MEINOLPH V. KAPPIUS
(MC) U.S.N.R., 1899-1946

CAPT. ALEXANDER A. ST. CLAIR,
M.C., A.U.S., 1911-1945

KILLED IN ACTION

Hilerd Westley Jenkins, River Forest, Ill.; aged 28; born in Forest Park March 6, 1914; University of Illinois College of Medicine, Chicago, 1938; interned at the Cook County Hospital in Chicago; member of the American Medical Association; entered active duty as a lieutenant in the medical corps of the U. S. Naval Reserve in December 1941 at the Naval Hospital in San Diego; on Dec. 9, 1941 assigned to the *Harris*, a hospital ship which during the ensuing months made numerous trips to Pearl Harbor; on Feb. 22, 1942 transferred to the destroyer U. S. S. *Worden* of the Pacific Fleet and in September 1942 to the U. S. S. *Monssen*, which on Nov. 13, 1942 engaged in battle with the enemy off Savo Island near Guadalcanal with great loss of life.

Meinolph Valen Kappius, Long Beach, Calif.; born in West Point, Neb. Feb. 23, 1899; Harvard Medical School, Boston, 1924; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; member of the American Medical Association and the Massachusetts Medical Society; formerly assistant in obstetrics at his alma mater and affiliated with Boston Lying-In and the Massachusetts General hospitals in Boston and the Free Hospital for Women; began active duty as a lieutenant commander in the medical corps of the U. S. Naval Reserve in April 1942; promoted to commander; officially reported missing in action Jan. 24, 1945, while attached to the U. S. S. *Kadashan Bay;* the plane in which he was flying was lost in the vicinity of the Admiralty Islands; the date of death was determined for administrative purposes within the Naval service to be Jan. 25, 1946, aged 47.

Correction.—Above is the correct photograph of Capt. Alexander A. St. Clair, M. C., A. U. S., who was reported missing in action on a flight over the Asiatic area July 13, 1943, and declared dead as of Dec. 19, 1945. In a number of copies of THE JOURNAL, September 18, page 227, Dr. St. Clair's obituary was printed under the picture of Comdr. Meinolph V. Kappius, M.C., U.S.N.R., whose obituary appears on this page.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 28, 1948.

Record Vital Statistics

During the war, with all its hardships and privations, British vital statistics actually showed an improvement. Now, when we are still suffering from the after-effects of the war in the form of scarcity and rationing of food, the same improvement continues. New low records for infant mortality, the general death rate and deaths from influenza in the first quarter of the present year are shown in the Registrar-General's returns, which have just been published. The provisional infant mortality rate was 41 per thousand live births, the lowest ever recorded for any first quarter. It was 11 below the figure for the same period last year and 25 below the average for the March quarters of the preceding ten years. It has already been announced that the provisional rate for the second quarter of this year is 31, the lowest on record for any quarter.

Births during the same period showed a rate of 18.9 per thousand compared with 17.8 for the preceding quarter and 22.8 for the corresponding quarter of 1947. The average birth rate for the first quarters of the five years 1942 to 1946 was 16.7. The death rate for the March quarter of 1948 was 12.4 per thousand, a new low record for that quarter. It compares with 17.1 for the corresponding quarter of 1947 and an average for the first quarters of 1942 to 1946 of 14.3. Deaths from influenza among civilians numbered only 644. The lowest number previously recorded in a first quarter was 1,470 in 1945, and the ten year average for first quarters of 1938 to 1947 was 3,800.

Two Healthy Young Cadets Die After an Eight Mile Training March

The country has been shocked by the deaths of two officer cadets, aged 19, during normal military training. They collapsed after an 8 mile route march partly over country and partly along roads, which had been arranged as part of their normal training. Each was in his thirteenth week of training. There was no specified time in which the march had to be completed. The syllabus, which had been carried out, included a 4 mile march without equipment but with rifles and a 2 mile march in battle order. Of the 32 members of the squad 3 were subsequently admitted to hospital, and of these the 2 mentioned died. At the coroner's inquest it was stated that the necropsies showed no signs of disease; the cadets were quite healthy. The only other factor was an exceedingly hot day. The verdict was death from heat stroke. No blame was attached to any one in command. But the War Office issued an order that exercises should be less stringent during the hot weather.

Shortage of Doctors and Excess of Applicants for Entry to Medical Schools

The National Health Service, which in one blow establishes medical socialism for the whole country, has come into force with remarkably little disturbance. Its efficacy, of course, depends on the quantity and quality of the doctors operating it. The former is certainly deficient. According to some only half the requisite number are available. There is no lack of entrants for the medical schools. The trouble is that the schools cannot immediately expand because laboratory and lecture room space is limited, as is the number of teachers. For each vacancy in the schools the applicants for entry range from 3 to 20, though this ratio exaggerates the excess because to an unknown extent some candidates apply to several schools. The difficult task of selection is carried out by the dean alone in half of the schools; at others by a committee. In an article devoted to student selection, *Lancet* declares that this has become harder than ever. For the coming year one London school has 700 applicants for 65 places, another 600 for 100 and a third 400 for 20 places. The question, "Is there any good reason for rejection?" has given way to "Is there any good reason for acceptance?" Methods vary widely. The universities require candidates to complete forms of questionnaires and a confidential report is then obtained from a head master or employer. Primary selection is made and then final selection by interview. The universities are so filled with students of this country that candidates from overseas, whether from the Dominions or Colonies or from foreign countries, can seldom be accepted.

An Operating Theater for the Training of Students

The Nuffield Operating Theater, specially designed for the training of students and for experiments in new surgical methods, was opened at Johannesburg by Sir Hugh Cairns, professor of surgery at Oxford University, who is on lecture tour in South Africa. It seems to be the only one of the kind in existence. It was designed by W. E. Underwood, professor of surgery in the University of Witwaterstrand. It will enable students to learn theater technic at their leisure, instead of in hospitals, where precision and speed are essential. It is a replica of the most modern hospital theaters.

ITALY

(From Our Regular Correspondent)

FLORENCE, Aug. 7, 1948.

Intoxication With Trinitrotoluene

At a meeting of the Association for Legal and Occupational Medicine presided over by Professor Palmieri, Drs. Caccuri and Sessa discussed intoxication by trinitrotoluene. They reported the results of research on 100 workmen who unloaded munitions in a dockyard near Naples. The workers were exposed to contact with trinitrotoluene either through the air because of the vapors, by the cutaneous route, or by the gastric route in the form of powder. The workmen had been exposed to trinitrotoluene for periods varying from three to ten months.

The symptoms reported were disturbances of the liver (pain, hepatomegaly, subicterus, or icterus); nervous disorders (headaches, vertigo, asthenia); disturbances of digestive apparatus (gastralgia, abdominal pains, anorexia, nausea, vomiting). Second in order were disturbances of the respiratory apparatus and of the cardiovascular apparatus (bradycardia, arterial hypotension).

Laboratory studies showed a positive Takata-Ara reaction and a positive Webster urine reaction in some of the cases, and an increase in azotemia in some cases. The examination of peripheral blood revealed a reduction of hemoglobin and a decrease of red blood corpuscles in nearly all persons studied, mild anisocytosis, then chylocytosis in many cases; normal or subnormal white blood cell counts; reduction of blood platelets in the great majority of the workmen and a definite increase in reticulocytes in 50 per cent of the persons studied. In nearly all persons there was a drop of the neutrophils containing pathologic granulations in the granulograms which were made according to the indications of Benda: the percentual number of intermediate form was predominant as compared to all the others; next in order were the normal forms, and last those of the extreme type. The pathologic neutrogranulogram may be considered as in close connection with the toxic injury to the peripheral blood and to the liver. The constancy of the observation makes it useful for early diagnosis of intoxication with trinitrotoluene and as an index of the degree to which the blood and the liver are affected.

At this meeting an order of the day was approved by which the Association of Legal and Occupational Medicine was held

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to vote that occupational medicine should be included as an obligatory branch of study in the last biennium at the medical faculty. At the great universities, schools for specialists of occupational medicine should be instituted and hygiene should become an obligatory branch of study at the industrial and technical intermediate schools.

Discussion on Immunology

At the Congress of the Salerno Medical and Surgical Association, Professors Califano and Merlino presented reports on the subject "Blood in the Light of New Knowledge." Professor Califano discussed the development of the concepts of immunology, emphasizing the nature of antibodies. Concerning gamma globulin he stated that one may think of it as a protein, the origin and significance of which have to do exclusively with immunity, and that since antibodies are constituted by gamma globulin or by components closely related to it, the problem identifies itself with that of the formation of serum globulin. There may be no doubt about the significance of lymphatic tissue in serologic immunity, although one must recognize always the important part of the reticulohistiocyte system in the genesis of the humoral immunity. The concept of elaboration of antibodies in strict dependence on protein alimentation may be considered as firmly grounded. The only alimentary factor which has an effect on the contents of antibodies in the serum is the amount of aminoacids in the diet.

In discussing the problem of blood transfusions, Professor Merlino pointed out the modern views on agglutinogens and agglutinins, on the Rh factor, and on the Hr factor.

The New Commissioner for Public Health

Professor Cotellessa, member of Parliament, has been nominated High Commissioner for Hygiene and Public Health. He started his scientific career at the hospital for infectious diseases "D. Cotugno" in Naples, then devoted himself to pediatry and as an assistant at the clinic of Naples and other Italian medical centers, becoming an associate professor in this speciality. He founded the Abruzzo section of the Pediatric Association and organized a service of consultation and assistance for the National Maternity and Child Welfare in the Province of Chieti.

BUENOS AIRES

(From Our Regular Correspondent)

Aug. 15, 1948.

Thoracic Esophagectomy and Neoplasm of the Esophagus

In the National Academy of Medicine of Buenos Aires Prof. Dr. Ricardo Finochietto, together with Dr. J. Horacio Resano, related the results in 100 patients who survived this operation. Since the first transthoracic esophagectomy done by him thirty years ago the good results have been obtained with better anesthesia, a better understanding of the physiology of operative shock and a better knowledge of surgical pneumothorax. Essential are the unlimited operative transfusion (according to the necessities of the patient), avoiding anoxia, and also standardization of the operation, trained personnel, appropriate instruments and antibiotics.

Of the 100 patients with cancer 50 were operable, but only 25 were resectable. For resection the authors fix an arbitrary limit: 7 cm. in the roentgenologic picture; in cases of greater tumors the resection is laborious or absolutely impossible. Neither the age nor bad general conditions are considered as absolute contraindications. The actual mortality is 40 per cent.

The authors are of the opinion that the Torek method leaves the patient practically invalid with few chances for normal deglutition; furthermore, 32 of the 33 patients who survived protested and wanted the artificial esophagus, only 1 being satisfied with the two fistulas. Seven of these 33 patients are alive. The maximum time of survival after esophagoplasty is two years.

The other terminal method, anastomosis, permits an immediate restoration of the deglutitive function; 22 of 67 patients treated by this method died of recurrences; the longest time a patient survived was four years and seven months. Of the 67 patients 47 were operated on according to the method of Biondi; 9 that of Garlock, and 11 that of Lewis.

The authors consider that the prolongation of life is greatest with resection of the tumor with transthoracic anastomosis.

Thyroid Insufficiency Due to Inhalation of Sulfonamide Drugs

Prof. Dr. E. B. del Castillo and his collaborators, Dr. F. Irigoyen and F. Vivone, observed 2 cases of thyroid insufficiency after prolonged inhalation of "prontosil" (an azosulfamide) due to working circumstances; only one of the patients had goiter. Both improved with thyroid medication. Such cases can be considered as professional accidents. It seems convenient that specialists of the respiratory tract control the thyroid function during prolonged treatment with sulfonamide nebulization.

Excretion of Pituitary Gonadotropins During Amenorrhea

In order to make a classification on a physiologic basis Drs. A. de la Balze and J. Argonz employed the test of pituitary gonadotropin in the urine (modification of the biologic method of Zondek) in 83 amenorrheic women. According to 155 tests of the follicle-stimulating hormone which had been carried out, these patients could be divided in three principal groups, according to the amount of this hormone (increased, diminished or normal). This method is considered useful and permits one to state in a case of amenorrhea the different types of gonadal insufficiency, the stage of the gonadotropic pituitary function and as result of these items, the physiopathologic diagnosis of the amenorrheas.

Pan-American Congress of Gastroenterology

The subjects for discussion, at this congress were mentioned in THE JOURNAL, June 12, page 659. The American guests, Drs. H. Bockus, C. A. Broders and B. B. Crohn, lectured also in the National Academy of Medicine, which designated them honorary members. Their contributions to the congress have been much esteemed. Other prominent lecturers came from Brazil, Chile, France, Mexico, Spain and Uruguay. The deliberations on the main subject, "Chronic Cholecystitis without Stones," took place under the chairmanship of Prof. Dr. Carlos Bonorino Udaondo, President of the National Academy of Medicine. The Interamerican Association of Gastroenterology has been founded, with headquarters in Buenos Aires. The second congress will be held in 1950 in Rio de Janeiro, with the main subject "Pathology of the Small Intestine."

Brief Items

The Argentine Society of Microbiology has been founded, with Prof. Dr. A. Bachman as president.——Dr. J. Taiana has been designated titular professor of thoracic surgery, as successor of Prof. José Arce.——A commission of experts has been created for studying the administration of streptomycin, under the chairmanship of Prof. Dr. Roque A. Izzo, Interventor of the Faculty of Medicine of Buenos Aires.——The Argentine League against Epilepsy has been founded, as a branch of the International League against Epilepsy; president is Dr. Aquiles Garciso, whose address is Argentine Medical Association, calle Santa Fe 1171, Buenos Aires.——The *Revista de Sanidad Aeronáutica* is a new trimonthly periodical, edited by the Dirección General de Sanidad de la Secretaría de Aeronáutica.

Correspondence

FURTHER NOTES ON MEDICAL EDUCATION IN GERMANY

To the Editor:—In the May 1, 1948 issue of THE JOURNAL, page 5, Dr. Irving S. Wright reported on the present status of medical education in Germany and Austria. It might be of general interest to supplement Dr. Wright's discussion with information concerning German efforts to improve the reported shortcomings. Originating with a request from German sources (particularly from the frequently mentioned Dr. F. Volhard), it was my mission to serve as a consultant of our military government to assist in the rehabilitation and reform of German medical schools. The German origin of the request was an invaluable help in overcoming the primary defense reaction toward suggestions proposed by one associated with medical education of an occupying power.

The main achievement of this mission was the establishment of an organization called Ausschuss für die Ausbildung und Fortbildung von Aerzten, an organization with aims similar to those of our Council on Medical Education and Hospitals. The present chairman of the Ausschuss is Prof. Kurt Felix, head of the Department of Vegetative Physiology at the University of Frankfurt am Main. This Ausschuss will meet every year on Ascension Day; its meetings are public, and participation is open to all members of the medical profession, including medical students. To everyone familiar with German medical education, the establishment of such an Ausschuss is a step forward that will make medical education in that country less autocratic and in general, of course, a step forward in making medical education in Germany a continuous problem, as it already is in this country. Founded only a year ago, the Ausschuss is still in its infancy.

FACULTIES

Appointment of part time clinical teachers, which has been more or less unknown in Germany in the past, is looked on with definite interest. The unfinished denazification procedures are a great obstacle in initiating such appointments as well as in sufficient staffing of the faculties in general. The denazification laws allow certain groups of persons to practice medicine, but do not allow them to teach. Other groups are permitted to do research, but again not to teach. Denazification laws are handled differently by the different occupation powers. German medical educators who are acceptable to one power are not acceptable to another. However, it is hoped that the denazification procedures will be finished this year. For security reasons, medical research projects must be submitted to the powers of occupation.

*Comparison of Minimal Hospital Bed Requirements for American Teaching Hospitals Serving Medical Schools with Facilities Available in German Medical Schools**

Service	American Standard (No. of Beds)	German Schools (Number of Beds)					
		Erlangen	Frankfurt	Heidelberg	Marburg	München	Würzburg
Internal medicine	300	367	355	290	150	500	176
General surgery	300	367	294	450†	300†	427†	221
Psychiatry	300	300	2655‡	297	85	3300	120
Pediatrics	150	130	85	198	145	505	260
Orthopedic surgery	60-80	20	250	635	104	397	200
Otolaryngology	60-80	90	107	...	...	200	83
Urology ‖	60-80	37	37	...	...	...	...
Ophthalmology	60-80	85	109	134	65	182	86
Neurology ¶	60-80	...	...	80	85	...	80
Gynecology	60-80	250	165	115	118	320#	110
Contagious Diseases							
Adults	100	15	80	...	30	...	57
Children	...	...	105	...	...	...	...
Tuberculosis							
Adults	100	28	102	...	40	...	26
Children	...	...	26	...	...	...	...
Obstetrics **	250††	25	111	75	40	...	130
Dermatology	...	...	482	200	...	167	...
X-Ray	...	...	20	75	...	...	...
Dentistry	...	...	...	36	...	...	...
Total	2,000	1,527	2,610	2,802	1,191	3,006	1,491

* American standard based on annual enrolment of one hundred new students, with not more than one hundred students in any of the advanced classes.
† Including urology.
‡ Including one hundred beds for neurology.
§ Including neurology.
‖ Combined with another service at Heidelberg, Marburg and München.
¶ Combined with another service at Frankfurt and München.
# Including obstetrics.
** Combined with another service at München.
†† Or enough to provide at least fifteen deliveries per student.

STUDENT BODY

It is assumed that the overcrowding of German medical schools will be over by the end of this year. Paradoxic as it may seem, it will not be possible to limit the number of students and to introduce student quotas on the basis of available facilities before the present overcrowding has passed. The reason for this delay is that the overwhelming majority of the present medical students are veterans, and it can be readily understood that any new procedure impeding economic adjustment of returning veterans would be inadvisable. Several causes have contributed to the present overcrowding of German medical schools. There was no deferment of German medical students during the war. The individual medical student received his education in leaps and bounds (educational furloughs). Therefore, at the present time, there are a great number of undergraduate medical students in various stages of education. This number is that much greater because the number of medical students increased appreciably during the war. Finally, far fewer examinations are given in the German medical curriculum than in the medical

curriculum of this country, and, thus, undesirable students are not eliminated. No medical examiner will let a student fail an examination the second time, particularly under pressing economic conditions, if that student has spent six years in the armed forces and from two to four years in a medical school. Most German veterans fall into this group.

RECONSTRUCTION OF GERMAN MEDICAL SCHOOLS

Reconstruction is in progress. Taking 1:1,000 as the optimal physician-patient ratio from both the professional and economic point of view, as well as accepting the present number of physicians as amply sufficient and the period of thirty years as the working time of a German physician, one would need for the American Zone, with its 17,000,000 inhabitants, 17,000 physicians to be replaced every thirty years, i. e., about 566 in one year. With six medical faculties in the American Zone (Erlangen, Frankfurt, Heidelberg, Marburg, München, Würzburg), that figure would require an entry class of about one hundred (100) students each year. The table gives the figures of the approximate number of hospital beds for a teaching hospital with an annual class of one hundred (100) students suggested by our Council on Medical Education and Hospitals as compared with the January 1948 figures of the University Hospitals in the American Zone.

CURRICULUM

German medical educators are interested in starting a reform. They are hesitant in beginning their experiment immediately for the following reasons. At present, graduation from any German medical school is recognized for the whole of Germany, i. e., not only by the different states within each zone of occupation but also by the individual states of all zones. Therefore, for the people of Germany medical licensure is still a keepsake and symbol of a unified Germany. Reform of a single medical school only—so desirable in starting a reform—faces the difficulty that graduates of this school may not obtain the licensure in other German states, but solely from the state in which the medical school is located. It may be added that in the Russian Zone of occupation the three single German states have a much lesser independent status than in the Western Zones and that the so-called German Central Administration in the Soviet Zone (an equal of which does not exist in the Western Zones) faces a much simpler problem. Plans for a reform in the Russian Zone have been published in *Das Deutsche Gesundheitswesen* (1:65-67, 1946; 1:566-568, 1946, and 1:597-600, 1946). It is interesting to note that such an outstanding German scientist as the well known pharmacologist Dr. W. Heubner of Berlin emphasized the similarity between the Russian and the American plans. It may also be pointed out that the Russian military government has a special medical educational section in its organization, which seems to be a constructive agent.

The great problem of medical education in Germany at the present time is the problem of postgraduate training. Attempts for such a program are being made in several places. The newly established exchange program (Chief Civil Affairs Division of the Army, Special Staff, U. S. Army, Washington 25, D. C.) might perhaps be utilized in this connection.

The Unitarian Service Committee, which has sent so many memorable American teaching teams to different European countries, will send one team to Germany this year. German medical educators also hope that it will be possible to establish closer contact with medical institutions of the U. S. Army in Germany.

OTTO E. GUTTENTAG, M.D.
University of California Medical School,
The Medical Center,
San Francisco.

SULFONAMIDE MIXTURES

To the Editor:—In the July 24 issue of THE JOURNAL there appeared a letter from Dr. David Lehr criticizing the conclusions of Zeller, Hirsh, Sweet and Dowling, who found that the disadvantages of using a mixture of sulfadiazine and sulfamerazine outweigh the advantages. Inasmuch as the article by Zeller and associates seemed to be a valid interpretation of carefully observed clinical phenomena, it is important to evaluate the usefulness of the sulfonamide mixtures from a theoretical point of view.

Although Lehr's observations on the independent solubilities of sulfonamide drugs are widely known and accepted, few persons realize how little there is to gain by using such mixtures. It is relatively simple to calcuate just how much extra sulfonamide compound can be dissolved through the use of the mixtures.

Without added alkali, the urine of the average patient with a bacterial infection is rather acid. For the sake of simplicity, let us assume that the p_H of the urine is 5.5, its volume 1,500 cc. and that acetylation of the sulfonamide compounds is complete. At p_H 5.5, the solubility of the acetylsulfadiazine is 20 mg. per hundred cubic centimeters and the solubility of acetylsulfamerazine is 38 mg. per hundred cubic centimeters (Gilligan, D. R.; Garb, S.; Wheeler, C., and Plummer, N.: Adjuvant Alkali Therapy in Prevention of Renal Complications from Sulfadiazine, J. A. M. A. 123:1160, 1943). Therefore, if 3 Gm. each of acetylsulfadiazine and acetylsulfamerazine is excreted per day in 1,500 cc. of urine at p_H 5.5, 300 mg. of acetylsulfadiazine and 570 mg. of acetylsulfamerazine will be in solution, while 2,700 mg. of acetylsulfadiazine and 2,430 mg. of acetylsulfamerazine will be in crystalline form. A total of 5,130 mg. of the sulfonamide mixture will be excreted as crystals, whereas if 6 Gm. of acetylsulfadiazine alone were excreted per day, 5,700 mg. would be in crystalline form.

Obviously, the difference between 5,130 and 5,700 is not a very significant one. Therefore, theoretical considerations corrobrate the clinical findings of Zeller and associates.

In addition, it should be pointed out that the solubility of acetylsulfadiazine at a p_H of 7.5 is 512 mg. per hundred cubic centimeters. Therefore, 7,680 mg. of it could be excreted in solution, without any crystal formation, in 1,500 cc. of urine at p_H 7.5.

The use of adjuvant alkali therapy with sulfadiazine alone is a much more effective way of reducing complications from sulfonamide compounds than the use of sulfonamide mixtures.

SOLOMON GARB, M.D.
LAURENCE A. JANOFF, M.D.,
New York.

Medical Motion Pictures

FILM REVIEW

As Others See Us. 16 mm., black and white, sound, 525 feet (1 reel), showing time fifteen minutes. Produced in 1945 by Associated Filmakers under a grant from the Becton, Dickinson Foundation for the American Hospital Association. Procurable on loan from: Department of Public Relations, American Hospital Association, 18 East Division St., Chicago 10.

This film tends to show the correct and the incorrect manner of receiving a patient on entrance to the hospital and providing for his comfort and care. It portrays the relationship of the hospital personnel with the patient and points out the importance of utilizing tact, kindness and consideration not only at the time of admission but throughout the entire period of hospitalization. There are a few sections in the film which may appear overemphasized; however, it should prove suitable for showing to all hospital personnel.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Privileged Communications: Statements Must Be Pertinent to Treatment.—This was an action by the administratrix of the estate of Edward C. Van Wie, deceased, to recover damages from the United States of America as a result of a collision between a motor vehicle operated by the deceased and a motor vehicle owned and operated by a rural mail carrier employed by the United States. The case was tried in the district court, N. D., Iowa, E. D.

Immediately following the collision the deceased was taken to a hospital at New Hampton, Iowa, and Dr. O'Connor, a practicing physician in that town, was called to attend him. At the trial, Dr. O'Connor was called as a witness by the defendant and was asked on direct examination as to what statements the deceased had made to him in relation to the collision and not connected with his treatment. The plaintiff objected to the testimony called for by the question on the ground that it concerned communications which are privileged under the Iowa law. The court reserved ruling, and Dr. O'Connor was permitted to testify that while the deceased was being treated he made the statement that "he did not see the vehicle which struck him." The question is as to the admissibility of this statement. Section 622.10, Code of Iowa 1946, provides in part as follows: "No practicing . . . physician, surgeon, or the stenographer or confidential clerk of any such person, who obtains such information by reason of his employment, . . . shall be allowed in giving testimony, to disclose any confidential communication properly entrusted to him in his professional capacity, and necessary and proper to enable him to discharge the functions of his office according to the usual course of practice or discipline. Such prohibition shall not apply to cases where the party in whose favor the same is made waives the rights conferred."

The federal courts follow the law of the forum as to communications privileged by state statutes. In the present case, said the court, Dr. O'Connor first saw the decedent in the emergency room at the hospital. He immediately began to administer to him, and the relation of doctor and patient then commenced. The statement in question was made by the deceased while he was being treated and, according to the doctor's testimony, at a time when the deceased was in a mentally clear condition. The statement was not, however, made in response to any question asked by the doctor, and the doctor admitted that the information conveyed by the statement was not necessary for purpose of treatment.

Statements of an injured person to his physician as to matters connected with the occasion out of which the injuries arose and observations by a physician of the patient and of the facts surrounding the injury would seem to stand or fall as privileged communications on their possible relevancy to treatment or on their relevancy as reasonably believed by either the physician or patient or both of them. While it is realized that it is common and natural human behavior for one in recounting a series of events which gave rise to an injury of a certain nature to include much data irrelevant to the ascertainment of the correct type of treatment to be administered, and while it is perhaps desirable that much latitude be allowed these statements as privileged communications to encourage disclosure of all facts necessary for treatment, an extension of the privilege to circumstances related by the patient which could have no possible bearing on the treatment of the injury or other professional service is beyond the plain language of the statute and the most liberal construction of it. It would not seem that whether or not the deceased saw the car which struck him could have any conceivable application to the determination of the proper treatment to be administered to him by Dr. O'Connor. It would not seem that such a revelation by the deceased could possibly have been considered by either communicant as reasonably necessary to the ascertainment of the injuries sustained and the correct treatment thereof. Nor would it seem that the statement was reasonably incident to any conversation which would bear so directly on the ascertainment of correct treatment as to be included as a part of a whole communication privileged by the statute. The statement was undoubtedly part of the normal reaction of a person in stating or discussing details of an unusual and hazardous incident which had just endangered his life. While the extent of his injuries at the time the statement was made were not fully known, the disclosure in no way could be calculated to bring them to light. In the cases in which the Iowa Supreme Court has held privileged certain statements to or observations by a physician regarding the facts of a mishap from which injuries requiring treatment were sustained, those statements or observations have been interpreted as being necessary to ascertain the proper treatment or the rendering of other professional service, or as having in some degree been regarded by the patient or physician as bearing on such treatment or service. In the present case, said the trial court, the statement in question was in no way necessary to be known in order for Dr. O'Connor to "discharge the functions of his profession according to the usual course of practice and discipline," and the decedent could not have reasonably believed that such a statement could have had pertinency to his treatment. The court therefore held that the statement was not a privileged communication under the Iowa statute in question and it was allowed to be admitted in evidence. The judgment of the trial court was in favor of the plaintiff. *Van Wie v. United States, 77 F. Supp. 22 (Iowa, 1948).*

Dental Practice Acts: Employment by Unlicensed Person as Ground for Revocation of License.—The defendant dentist was charged with a violation of the New Jersey dental practice act and, after a hearing by the state board of registration and examination in dentistry, was found guilty and his license was suspended for six months. This ruling was reversed by the trial court on the ground that the statutory provision under which his license was suspended was unconstitutional, so the state board appealed to the Court of Errors and Appeals of New Jersey.

The dental practice act of New Jersey authorizes the revocation or suspension of a license to practice dentistry if the licentiate has been found guilty of having "been employed by an unlicensed manager, proprietor, operator or conductor . . ." The question which we shall answer, said the court, is whether a license to practice dentistry may constitutionally be revoked on a justified finding that the licensee has submitted to employment as a practicing dentist by an unlicensed person. The dental practice act of New Jersey, in addition to the above mentioned provision, also provides that no person shall practice dentistry unless licensed to do so and that any person shall be regarded as practicing dentistry within the meaning of the act who is manager, proprietor, operator or conductor of a place where dental operations are performed. The constitutionality of these latter statutory provisions is not disputed, nor could it well be, the court continued, for the restrictions so imposed upon personal liberty of actions are within the police power of the state to provide for the general welfare of its people and to that end to prescribe all such regulations as in its judgment will secure or tend to secure them against the consequences of ignorance and incapacity as well as of deception and fraud. The practice of dentistry has points of close contact with that of medicine, which has long been the subject of careful supervision and control. Since it is within the power of the state to provide that no unlicensed person shall be the manager, proprietor or conductor of a dental office, continued the Court of Errors and Appeals, it seems to us to be also within the power of the state to provide, conversely, that a licensed dentist shall not be employed in a dental office by an unlicensed manager, proprietor or conductor and to enforce that prohibition by revoking or suspending the license of an offending licensee. Accordingly the court held that the provision of the dental practice act prohibiting employment of a licensed dentist by an unlicensed person was constitutional and that the state board of registration and examination in dentistry was authorized to suspend a license on such a ground.—*Taber v. State Board of Registration & Examination in Dentistry, 59 A. (2d) 231 (N. J., 1948).*

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Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American J. Obstetrics and Gynecology, St. Louis

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Now and Then. Statistical Review of Progress of Midwifery During Last Twenty Years with Thoughts for Future. W. F. T. Haultain. —p. 733.

Benign Trophoblastic Cell Proliferation. C. G. Tedeschi and A. A. Matarese.—p. 758.

*Early Rising After Delivery. E. L. Cornell and J. J. Mullen.—p. 768.

*Acute Puerperal Mastitis: Clinical and Bacteriologic Studies in Relation to Penicillin Therapy. H. C. Hesseltine, C. G. Freundlich and K. Eileen Hite.—p. 778.

Ovarian Dysfunction in Young Women Treated with Low-Dosage Irradiation. Della G. Dripps.—p. 789.

Fear, Important Etiologic Factor in Obstetric Problems. H. C. Walser. —p. 799.

*Spinal (Saddle Block) Anesthesia in Obstetrics. G. J. Andros, W. J. Dieckmann, P. Ouda and others.—p. 806.

Use of Vaginal Smear in Gynecologic Service. L. L. Mackenzie, B. B. Wetchler, J. C. DuBois and T. Neustaedter.—p. 821.

Preinvasive and Invasive Carcinoma of Cervix Uteri: Pathogenesis, Detection, Differential Diagnosis, and Pathologic Basis for Management. E. R. Pund, J. B. Nettles, J. D. Caldwell and H. E. Nieburgs. —p. 831.

Spectroscopic Detection of Hematin in Peripheral Blood: Aid to Diagnosis of Ruptured Tubal Pregnancy. F. E. Whitacre, H. D. Lyna, and D. B. Morrison.—p. 838.

Study of Incidence and Occurrence of Symptoms of Vaginal Trichomonads and Various Species of Yeast in Pregnancy. C. G. Johnson and Ruth Mayne.—p. 852.

Study of Use of Penicillin in Premature Rupture of Membranes. J. H. E. Woltz and T. S. Stashak.—p. 859.

Splenectomy in Pregnancy: Its Hematologic Indications and Obstetric Management. A. C. Barnes and C. A. Doan.—p. 864.

Sterilization Failure with External Migration of Ovum. I. F. Stein, M. R. Cohen and R. Elson.—p. 875.

Combined Local Infiltration Anesthesia and Pentothal Sodium Anesthesia in Cesarean Sections: A Preliminary Report. J. A. Fino and J. R. Eisaman.—p. 887.

Cervical Cancer with Metastasis to Breast. H. Speert and A. V. Greeley.—p. 894.

Early Rising After Delivery.—Cornell and Mullen report 1,000 patients admitted to Henrotin Hospital for delivery who represent a typical cross section of postpartum cases. They were allowed up on the sixth day or earlier, 80 per cent being up prior to the fifth day. These patients were in better condition at the time of discharge than if they had remained in bed for eight or more days. They were in a position to adapt themselves more readily to their daily household routine. Episiotomy wound healing was not adversely affected, nor was morbidity increased. No case of thrombophlebitis occurred in those delivered vaginally, which suggests that the tendency toward this complication was reduced. There was no case of uterine prolapse. The rate of involution of the uterus was increased. When necessary, because of overcrowding, the patient could be discharged from the hospital earlier than heretofore with a greater margin of safety. The postoperative course of the 53 cases of cesarean section included in this group was more nearly uneventful. Distention was infrequent. The necessity for catheterization and enemas was lessened when the patient was up to the toilet on the first postoperative day. One case of thrombophlebitis occurred thirty days after operation.

Acute Puerperal Mastitis.—Hesseltine and his co-workers report observations on 210 patients with suppurative puerperal mastitis observed at the Chicago Lying-in Hospital during the last thirteen and one-half years. Six of these patients belonged to a group of 23 with acute puerperal mastitis treated with penicillin only. In these 6 symptoms had existed from twenty-four to one hundred and forty-four hours before the initiation of the penicillin therapy, whereas the longest period preceding treatment in the 17 nonsuppurative cases was forty hours. All 23 patients became afebrile within forty-eight hours, but this is not proof that the patient has been completely cured, as is shown by the occurrence of abscess in 6 patients during treatment. Penicillin resistance was studied in eleven strains of staphylococci isolated from suppurative mastitis. These grew in the presence of 0.006 to 6.25 units per cubic centimeter of penicillin. A significant proportion of these strains were resistant to the antibiotic, since four grew in at least 3.1 units per cubic centimeter. The local use of ointment containing penicillin on the nipple after nursing failed to affect the incidence of mastitis in postpartum patients. Nasopharyngeal cultures from mothers and babies were examined for Staphylococcus aureus. Twenty-one of 30 babies were found to harbor Staph. aureus during the first ten days of life, as were 20 of the 30 mothers. Ten of these strains were resistant to 0.5 or more units per cubic centimeter of penicillin in vitro. This resistance would appear to be a factor in the development of suppuration during treatment with penicillin and should be considered in the determination of "adequate" penicillin therapy. Infection of the breast may occur in lactating mothers from the patient herself or from the nursing infant. Although the importance of the nasopharynx is suggested, other possible sources of infection must be recognized. Late treatment, the resistance of some staphylococcus strains to penicillin and the localizing effect of the inflammatory tissue would seem to contribute to the progression of the disease process to suppuration. Increased dosage of penicillin seems desirable for infections with organisms of higher than usual resistance to the antibiotic.

Spinal Anesthesia in Obstetrics.—Andros and his co-workers practiced saddle block anesthesia in 719 parturient women between the ages of 18 and 42 years, at the Chicago Lying-in Hospital, during the first four months of 1947. The majority of the injections were made with the patient in her labor bed, placed in a sitting position over the side of the bed, bending forward and supported by an assistant. Spinal puncture was made at the level of the fourth lumbar interspace. The anesthetic agents used were difucaine hydrochloride in 514 instances, tetracaine hydrochloride in 115 cases, procaine hydrochloride in 27 and "metycaine hydrochloride" in 47. Seven additional patients received butethamine formate ("monocaine formate"). In 24 of the 719 cases (3.3 per cent) there was failure to obtain anesthesia. Fourteen of these failures were converted to successes by repetition of the tap and the injection. In this series of 709 patients successfully anesthetized there were 346 primiparas and 363 multiparas. Anesthesia was instituted at 5 or 6 cm. of cervical dilatation in multiparas and near 8 cm. in primiparas. Other prerequisites to saddle block should be progressive labor, an effaced cervix, fixation of the fetal head and no cephalopelvic disproportion. The usual duration of complete uterine analgesia obtained from procaine hydrochloride and "metycaine" was from sixty to ninety minutes, with perineal anesthesia usually lasting nearly two hours. Tetracaine generally gave uterine analgesia of ninety to one hundred and five minutes, and perineal anesthesia between two and two and one-half hours. Only single blocks were used in the great majority of patients. Excluding the 14 patients receiving two taps for a single successful anesthetic, there were 65 patients who received the benefits of two or three successful injections; these patients were carried under saddle block anesthesia from three hours to slightly less than nine hours when delivery was completed. The procedure has been found to be safe, simple and precise. The degree of success has been high. The rate of operative intervention in delivery was not significantly increased. Complications attributable to the anesthetic procedure have not been a problem. The benefits to the fetus in early spontaneous respiration have been striking. There has been no increase in the fetal or maternal morbidity or mortality.

American Journal of Ophthalmology, Chicago

31:527-666 (May) 1948

Fat Embolism Involving the Human Eye. M. H. Fritz and M. J. Hogan.—p. 527.
Teaching of Ophthalmology (The Harry S. Gradle Lecture). D. Vail.—p. 535.
Monocular Operation for High Divergent Strabismus. L. Weekers.—p. 541.
Military Ophthalmology in the European Theater. D. Marshall.—p. 545.
*Cancer and the Lens. E. Sachs and R. L. Larsen.—p. 561.
Recording of Visual Fields. M. Chamlin.—p. 565.
Stereophotogrammetric Study of Anterior Segment of Eye. E. V. Bertotto.—p. 573.
Ocular Syndrome of Cataract and Papilledema in Manifest Form of Parathyroid Deficiency. D. J. Lyle.—p. 580.
Extraction of Cataract in Presence of Fluid Vitreous. D. B. Kirby.—p. 585.

Cancer and the Lens.—Sachs and Larsen say that cancer of the lens has never been observed. They inquire as to the anticarcinogenic factors which render the lens immune to cancerous invasion. They discuss factors of biologic, metabolic, physical and chemical nature—any or all of which may be responsible for the nonexistence of cancer in the lens.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

59:617-770 (May) 1948

Cerebral Angiography: Clinical Evaluation Based on 107 Cases. J. R. Green and R. Arana.—p. 617.
Roentgen Considerations of Pyelonephritis in Small Kidneys. E. P. Pendergrass, R. H. Chamberlain and F. P. Brooks.—p. 651.
Roentgenologic Manifestations of Intrathoracic Injury Due to Missiles. W. A. Evans Jr.—p. 662.
Pulmonary Cavities "Below the Diaphragm": Phenomenon Sometimes Seen in Pneumoperitoneum Treatment of Pulmonary Tuberculosis. P. Morgenstern and I. Pine.—p. 677.
Gastric Tuberculosis: Case Report. H. R. Morris.—p. 682.
Tumors of Small Intestine. Report of 2 Cases of Carcinoma of Jejunum. P. Delano.—p. 685.
Simplified Method of Roentgen Pelvicephalometry. A. K. Wilson.—p. 688.
Solitary Unicameral Bone Cyst of Right Ilium. Case Report. G. W. Heublein and C. L. Baird.—p. 699.
Agenesis of Vertebral Bodies—Cause of Dwarfism. Margaret J. Giannini, F. J. Borrelli and W. B. Greenberg.—p. 705.
Isolated Dislocation of Lesser Multangular Bone. D. A. Sampson.—p. 712.
Granulosa Cell Tumor of Ovary with Special Reference to Radiosensitivity. R. D. Moreton and E. T. Leddy.—p. 717.
Comparison of Intradermal and Ocular Methods of Testing for Sensitivity to Diodrast. A. G. Singer Jr.—p. 727.
Roentgen-Ray Calibration of Photographic Film Exposure Meter. L. J. Deal, J. H. Roberson, and F. H. Day.—p. 731.

Annals of Western Medicine & Surgery, Los Angeles

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Grave Prognosis of Appendicitis in the Aged. D. C. Collins.—p. 193.
Anorectal Fistula: Historical Baeground and Modern Treatment. H. M. Young.—p. 206.
Nonsurgical Treatment of Genital Relaxation: Use of Perinecometer as Aid in Restoring Anatomic and Functional Structure. A. H. Kegel.—p. 213.
*Solar Retinitis Due to Exposure During Eclipse. P. Tower.—p. 217.
Solar Eclipse and Vision. D. M. Harwood.—p. 222.

Solar Retinitis Due to Exposure During Eclipse.—Tower says that within two weeks following a recent solar eclipse, 8 children presented themselves at the eye department of Yale Street Health Center with signs of retinal injury to the region of the macula, due to exposure to the sun. The symptoms of solar retinitis are a persistent after-image, positive scotoma and metamorphosia. Visual acuity is reduced. Ophthalmoscopic examination at first may reveal no abnormality or only a pale spot at the fovea centralis surrounded by a brownish ring. Subsequently, a translucent gray spot, suggestive of congestion and surrounded by a darker ring, may become visible in the center of the macula lutea. The pigment deposits become more pronounced and form a circular stippled area of gray around the fovea centralis. The damage proved to be irreversible in all children. Vision had not returned to its previous state after a lapse of several months. Neither smoked glasses nor photographic film afford sufficient protection for observing an eclipse. Ordinary sun glasses, when used for looking into the sun, transmit infra-red rays. The incidence of solar retinitis decreases with advancing age; school children are most likely to experience macular injury following observation of an eclipse.

Blood, New York

3:471-616 (May) 1948

Chemical Specificity of Interaction of Diverse Human Plasma Proteins. E. J. Cohn.—p. 471.
Span of Life of Red Blood Cell: A Résumé. Winifred Ashby.—p. 486.
Studies on Free Erythrocyte Protoporphyrin, Plasma Iron and Plasma Copper in Normal and Anemic Subjects. G. E. Cartwright, C. M. Huguley Jr., Helen Ashenbrucker and others.—p. 501.
Studies in Iron Transportation and Metabolism: VI. Absorption of Radio-Active Iron in Patients with Fever and with Anemias of Varied Etiology. Reubenia Dubach, Sheila T. E. Callender and C. V. Moore.—p. 526.
Osometric Behavior of Normal and Abnormal Human Erythrocytes. G. M. Guest.—p. 541.
Method for Determining the Form of Distribution of Red Cell Resistances to Simple Hemolysins. E. Ponder.—p. 556.
Hemoglobin Healthy College Undergraduates and Comparisons with Various Medical, Social, Physiologic and Other Factors. C. W. Heath.—p. 566.
Studies of Staphylococcagulase Reaction: Nature and Properties of Plasma Activator and Inhibitor. M. H. Kaplan and W. W. Spink.—p. 573.
Some Hematologic Effects of Irradiation. W. Bloom and L. O. Jacobson.—p. 586.
Effect of Radiation on Hemopoiesis: Is There an Indirect Effect? J. S. Lawrence, W. N. Valentine and A. H. Dowdy.—p. 593.
Normal Blood Counts in Different Seasons. J. E. Holm and A. A. Videback.—p. 612.

Bulletin of Johns Hopkins Hospital, Baltimore

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Total Intravenous Alimentation: Its Effect on Mineral and Bacterial Content of Feces. L. E. Duncan Jr., G. S. Mirick and J. E. Howard.—p. 515.
British National Health Service. W. Jameson.—p. 529.
*Familial Spread of Vaccinia with One Death: Isolation and Identification of Virus. Frieda G. Gray.—p. 538.
Reduction of Intussusception by Hydrostatic Pressure: Experimental Study. M. M. Ravitch and R. M. McCune Jr.—p. 550.
Audiometry with Use of Galvanic Skin Resistance Response: Preliminary Report. J. E. Bordley, W. G. Hardy and C. P. Richter.—p. 569.

Familial Spread of Vaccinia.—Grey reports the spread of vaccinia from a recently vaccinated child to 3 other members of the family. The virus was isolated from 2 of these patients and was identified as vaccinia by neutralization and immunity tests. Sixteen successive rabbit passages were carried out with the virus isolated from the fatal case. Intracytoplasmic inclusion bodies were demonstrated in the cutaneous lesions of the fatal case and of inoculated rabbits.

Cincinnati Journal of Medicine

29:257-316 (May) 1948

The Hippocratic Oath in Modern Dress. M. Levine.—p. 257.
Antibiotics in Treatment of Venereal Diseases. J. E. Moore.—p. 263.
Improved Housing and Slum Eradication. W. B. Bean, N. J. Giannestras and G. Lowenthal.—p. 271.

Journal of Allergy, St. Louis

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Immunochemical Aspects of Allergy. D. H. Campbell.—p. 151.
Thermolability of Artificially Stimulated Human Antibodies. W. B. Sherman, R. A. Cooke, S. B. Crepea and Lillian M. Downing.—p. 160.
*Growth Patterns of Allergic Children: Statistical Study Using Grid Technic. M. B. Cohen and L. E. Abram.—p. 165.
Induction of Asthmalike Attacks in Subjects with "Idiopathic" Asthma. F. C. Lowell and I. W. Schiller.—p. 172.
Comparative Studies of Several Antihistaminic Drugs. C. E. Arbesman.—p. 178.
Pharmacologic Characteristics of Neohetramine: New Antihistaminic Drug. J. V. Scudi, J. F. Reinhard and N. B. Dreyer.—p. 184.
Device for Electrostatic Precipitation of Bacteria and Fungus Spores Upon Culture Plates. R. Rooks.—p. 200.
Device for Electrostatic Precipitation of Pollen and Fungus Spores Upon A Counting Slide. R. Rooks.—p. 206.

Growth Patterns of Allergic Children.—Cohen and Abram raise the question of the existence of fundamental characteristics which distinguish allergic persons from the general population and their hereditary patterns. Previous studies have indicated that the allergic child is likely to be retarded, short for his age and light for his height when compared with average standards for height and weight. This has been thought to be due to the effects of the disease on appetite or to some actual disturbance in the utilization of food associated with the disease. It is possible that allergy occurs in children who have physical potentialities as regards body type and growth different from those of the nonallergic population, but until recently there have been no satisfactory methods for studying these possibilities.

The grid technic described by Wetzel makes such a study possible. From 503 observations on 150 allergic children seen in private practice compared with 622 observations on 102 nonallergic controls studied by the grid method, the authors draw the following conclusions: 1. Allergy occurs more frequently in children (especially boys) who, by inheritance, are constitutionally slender. 2. Allergy is a common cause of growth failure. 3. Control of active allergy is accompanied by a corresponding growth repair provided an adequate diet is available.

Journal of Bacteriology, Baltimore

55:581-768 (May) 1948. Partial Index

Antibiotic Substances Separated from Sumac. H. J. Carlson, H. G. Douglas and H. D. Bissell.—p. 607.
Antibiotic Agents Separated from Root of Lace-Leaved Leptotaenia. H. J. Carlson and H. G. Douglas.—p. 615.
Interference Between Human Pneumonitis Virus and Psittacosis Virus. O. J. Golub and J. C. Wagner.—p. 627.
Activation of Bacterial Virus T4 by L-Tryptophan. T. F. Anderson. —p. 637.
Inheritance of Requirements for Absorption Cofactors in Bacterial Virus T4. T. F. Anderson.—p. 651.
Influence of Temperature and Nutrients on Plaque Formation by Bacteriophages Active on Escherichia Coli Strain B. T. F. Anderson. —659.
Cultural Characteristics of Donovania Granulomatis. G. Rake and J. J. Oakay.—p. 667.
Effect of Sodium Fluoride on Metabolism of Certain Mycobacteria. R. J. Fitzgerald and F. Bernheim.—p. 677.
Metabolism of Biotin and Oxybiotin by Lactobacillus Pentosus 124-2. Kratha K. Krueger and W. H. Peterson.—p. 693.
Effect of Radioactive Phosphorus on Suspension of Escherichia Coli. C. F. Schmidt.—p. 705.
Antigenic Studies of Group of Paracolon Bacteria (Bethesda Group). P. R. Edwards, Mary G. West and D. W. Bruner.—p. 711.
Identification of Antibiotics by Means of Resistant Strains of Bacteria. P. G. Stansly.—p. 721.
Cytochemical Mechanisms of Penicillin Action. VI. Influence of Cobalt on Optimal Bacteriostatic Concentration of Penicillin. R. Pratt and Jean Dufresney.—p. 727.
Grisein, Antibiotic Produced by Certain Strains of Streptomyces Griseus. D. M. Reynolds and S. A. Waksman.—p. 739.
Preliminary Observations on Germination of Spores of Bacillus Mycoides in Nitrogen-Free Medium and Certain Properties of Transparent Cells. G. Knaysi.—p. 753.

Journal of Gerontology, Springfield, Ill.

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Use of Drosophila Melanogaster as Screening Agent for Longevity Factors. T. S. Gardner.—p. 1.
Who Is Old? Death Rate in Japanese Concentration Camp as Criterion of Age. R. A. M. Bergmann.—p. 14.
Maturity and Ageing. Course in Institute of Child Welfare of University of Minnesota. D. B. Harris.—p. 18.
Effects of Progesterone, Estradiol, Thyroid Hormone, and Androsterone on Artificial Premature "Climacteric" of Pure Gonadal Origin Produced by Ovariectomy in Rats. V. Korenchevsky and Vera E. Jones. —p. 21.
*Effect of Arteriosclerosis on Dynamics of Hypertension in Aged: Preliminary Clinical and Pathologic Study of 150 Cases. F. D. Zeman and R. M. Schwartz.—p. 40.
Observations in Old Age Counselling Center: Preliminary Report on First 100 Clients. K. Stern.—p. 48.

Effect of Arteriosclerosis on Hypertension in the Aged.—Zeman and Schwartz made blood pressure studies on 150 elderly persons and correlated them with the findings at necropsy. Factors influencing blood pressure are evaluated with emphasis on the effect of the sclerotic aorta and its branches in producing the low diastolic pressures often found in aged persons. The patients were residents of the Home for Aged and Infirm Hebrews of New York City. The series included 66 men and 83 women, ranging in age from 60 years to 92 years. The patients were observed from a few days to twenty years. Blood pressure is mainly determined by four variables: the cardiac output, peripheral resistance, aortic elasticity and capacity. As age advances, there is a tendency for peripheral resistance to increase, for aortic elasticity to decrease, for aortic volume to increase and for cardiac output to decrease. A "normal" blood pressure in old age is not evidence of a normal cardiovascular system, but is the result of several of the aforementioned factors acting in opposite directions. Systolic hypertension is not to be sharply distinguished as a special form of elevated blood pressure, entirely normal for old age, and benign. Many cases of so-called systolic hypertension are in reality a form of systolic-diastolic hypertension in the sense that peripheral resistance is increased, but the level of diastolic pressure is modified by changes in the great vessels. Systolic and diastolic hypertension in old age appears to make the persons who manifest it more liable to cerebral accidents and adds a burden to the heart. Malignant hypertension is rarely, if ever, observed in the aged. The level of blood pressure in old age should be supplemented by studies to determine the cardiac, cerebral and renal function and the degree of elasticity and dilatation of the aorta. Physiologic measurements of the cardiac output and peripheral resistance would be particularly desirable.

Journal of Nervous and Mental Diseases, New York

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Bilateral Fractional Resection of Frontal Cortex for Treatment of Psychoses: Preliminary Report. R. G. Heath and J. L. Pool.—p. 411.
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Kentucky Medical Journal, Bowling Green

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Cancer of Female Generative Organs. A. N. Arneson.—p. 146.
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Needle Biopsy in Diagnosis of Liver Disease. L. Dickinson.—p. 182.
Uveitis and Secondary Glaucoma. W. D. Frey.—p. 185.
Intrathoracic Esophagogastric Anastomosis for Carcinoma of Lower Esophagus and Cardiac End of Stomach. F. W. Rankin and L. E. Hurt.—p. 188.
Rheumatic Fever in Children. R. E. Kinsey.—p. 193.
Types of Fixation Indicated in Open Reduction. C. G. Follis.—p. 195.

Medical Annals of District of Columbia, Washington

17:257-310 (May) 1948

*Transorbital Lobotomy: Preliminary Report of 10 Cases. W. Freeman. —p. 257.
Statistical Analysis of Deaths Among Diabetics in District of Columbia for Period 42 Years (1903-1944 Inclusive). J. A. Reed.—p. 262.
Colpocytological (Papanicolaou) Method of Diagnosis of Uterine Cancer: Preliminary Report. J. K. Cromer, Lois I. Platt and T. Winship. —p. 272.
Neuritides of Mechanical or Pressure Origin. F. R. Riesenman.—p. 277.
Toothpick in Peritoneal Cavity: Report of Case. W. J. B. Orr.—p. 283.

Transorbital Lobotomy.—Freeman reports 10 cases of transorbital lobotomy followed for two years. There was 1 instance of left hemiparesis of four days' duration with complete recovery of power on that side. Later this patient had epileptic seizures. The other 9 patients suffered no ill effects. One of the patients died twenty months after operation of carcinoma of the pancreas. Of the 9 living patients, 5 are keeping house, 2 are employed, 1 is living at home and 1 relapsed eighteen months later. Transorbital lobotomy has a place in the treatment of mental disorders somewhere between shock therapy and major frontal lobotomy. It is to be considered in the case of schizophrenic patients who have been sick less than a year and who respond unfavorably to shock therapy. It may be tried in cases of involutional depression with agitation when shock therapy fails. If transorbital lobotomy produces only temporary results, standard frontal lobotomy may give permanent relief. Transorbital lobotomy does not seem to produce the undesirable effects that sometimes follow frontal lobotomy. Part of this is due to the less extensive character of the operation.

Military Surgeon, Washington, D. C.

102:335-426 (May) 1948. Partial Index

Medical Cooperation in Civil Defense. G. E. Armstrong.—p. 335.
Training Activities of Army Medical Department. R. E. Duke.—p. 339.
Medical Problems of Future Submarines. O. D. Yarbrough.—p. 342.
Multiple Neurofibromatosis Involving Urinary Bladder. J. C. Kimbrough, J. N. Furst and D. K. Worgan.—p. 346.
*Successful Treatment of Case of Uremia by Means of Peritoneal Irrigation. R. H. Allbee and J. L. Mayfield.—p. 348.
Treatment of Traumatic Aphasics of World War II at Birmingham General V. A. Hospital, Van Nuys, California. J. M. Nielsen, D. A. Schultz, Marria Lennon Corbin and Aleen Crittsinger.—p. 351.
Neuropsychiatric Activities at Darnall General Hospital. T. C. C. Fong.—p. 365.
Local Control of Epidemic Dengue Fever. R. P. Holdsworth, Jr.—p. 377.
Improved Operation for Ingrowing Toenail. W. L. Gist.—p. 381.

Peritoneal Irrigation in Uremia.—Allbee and Mayfield treated 1 man aged 45 who had uremia due to acute renal failure of undetermined cause by peritoneal irrigation, using Ringer's solution and later distilled water and 5 per cent dextrose. Irrigation was instituted after patient had been anuric for nine days. It was continued for ten days; on the tenth day the kidneys had a twenty-four hour output of 1,700 cc. This method provided a substitute for the function of the kidneys by keeping the nitrogenous products from increasing and by even decreasing them a little over this ten day period until the damaged kidneys could regain function. The technical aspects of the method did not prove to be difficult, and there was no peritonitis of note. Peritoneal irrigation was a life-saving measure in this case; it is recommended that it be tried in similar cases.

Missouri State Medical Assn. Journal, St. Louis

45:321-400 (May) 1948

Cancer of Colon and Rectum: Current Trends in Surgical Management. J. Modlin.—p. 339.
Tumor Seminar: Embryonal Adenoma of Thyroid with Blood Vessel Invasion. S. Warren.—p. 345.

45:403-464 (June) 1948

Pulmonary Histoplasmosis. B. M. Stuart, J. W. Gardner, D. V. LeMone and A. C. Van Ravenswaay.—p. 417.
Complications in Treatment of Fractures by External Skeletal Fixation. J. A. Key.—p. 422.
Treatment of Acute Cholecystitis. J. H. O'Neil.—p. 425.
Supernumerary Kidney with Ectopic Ureteral Orifice. J. J. Cordonnier and W. C. Scrivner.—p. 430.
False Positive Serologic Tests for Syphilis. H. L. Joseph.—p. 434.

New England Journal of Medicine, Boston

238:679-722 (May 13) 1948

Whither the Pegasus of Public Health? H. Emerson.—p. 679.
Reconstruction of Burned Hand. R. C. Tanzer.—p. 687.
Pheochromocytomas Coexisting in Adrenal Gland and Retroperitoneal Space, with Sustained Hypertension: Report of Case with Surgical Cure. E. J. Ganem and G. F. Cahill.—p. 692.
Orthopedic Surgery: I. Conditions of Shoulder. C. B. Larson.—p. 697.
Pelvic Abscess: Multiple Brain Abscesses.—p. 703.
Malignant Teratoma of Anterior Mediastinum, Involving Pericardium, Pleura and Right Lung.—p. 706.

New Jersey Medical Society Journal, Trenton

45:223-272 (May) 1948

Cancer Program in New Jersey: IV. Financial Aid for Service to Cancer Patients. W. M. Wuester and O. R. Holters.—p. 226.
Gastro-Intestinal Bleeding Produced by Ulcerated Meckel's Diverticulum. A. J. Barbano.—p. 232.
Propyl Thiouracil in Hyperthyroidism. W. A. Crist.—p. 234.
*Severe Nasal Congestion Following Use of Naphazoline ("Privine") Nose Drops. W. G. Talmage.—p. 237.
Evaluation of Immunity to Whooping Cough. G. A. Maggio.—p. 239.

Severe Nasal Congestion Following Use of Nose Drops.—Talmage reports the case of a woman, aged 62, who came to him complaining that her "nose was blocking up" continually. More than a year before, a specialist had prescribed a 0.1 per cent solution of naphazoline hydrochloride. The brand used was "privine hydrochloride" (N. N. R.), which was available in 0.1 per cent and 0.05 per cent solutions. The manufacturers advised that only the weaker solution should be used when prescribed for self application. In this case, it was intended for use during an acute infection of the upper respiratory tract, and the stronger (0.1 per cent) solution was prescribed. The patient continued the drops long after original need for them should have disappeared. For more than a year she had been using 1 ounce a week. Her eyelids were puffy. Nasal mucosa and turbinates were red and extremely dry but appeared unusually congested and swollen. Believing that the long-continued use of the naphazoline might account for the nasal congestion and nervousness, the author instructed her to discontinue the nose drops. The feeling of apprehension and dependence on the naphazoline completely subsided after three weeks. The author mentions others who have observed numerous patients whose nasal congestion had been aggravated or maintained by naphazoline. Vasodilatation is probably a compensatory reaction to the initial vasoconstriction produced by this drug.

New York State Journal of Medicine, New York

48:817-960 (April 15) 1948

Choice of Procedure in Ophthalmic Plastic Surgery. A. E. Sherman.—p. 861.
Observations on Neurogenic Bladder. W. F. Whitmore and L. M. Isales.—p. 869.
Results of Radiation Therapy of Bladder Cancer. V. F. Marshall.—p. 875.
Transurethral Treatment of Bladder Tumors. A. M. McLellan.—p. 876.
Segmental Resection of Bladder for Cancer. J. Edwin Drew.—p. 877.
Ureterocutaneous Anastomoses. G. A. Humphreys.—p. 879.
Results of Ureterointestinal Anastomoses. M. Schnittman.—p. 882.
Total Cystectomy. W. F. Whitmore Jr. and Neil P. Beal.—p. 884.
Summary and Conclusions. V. F. Marshall.—p. 887.
Streptomycin in Clinical Tuberculosis. C. Muschenheim, W. McDermott and P. A. Bunn.—p. 889.
Diagnostic Difficulties in Intrathoracic Neoplasms. J. L. Pool.—p. 895.
Diagnosis and Treatment of Minimal Tuberculosis. D. R. McKay.—p. 899.
Isolated Nonpenetrating Injuries of Pancreas: 10 Year Review of Literature and Report of a Case. J. F. Hart and J. R. Lisa.—p. 903.
Diagnosis of Sickle Cell Anemia. W. J. Doyle and J. Battaglia.—p. 907.

Northwest Medicine, Seattle

47:241-312 (April) 1948

Differential Diagnosis and Treatment of Leukemias. E. E. Osgood.—p. 257.
Rheumatoid Spondylitis: Its Early Diagnosis and Treatment. S. E. Rees, E. A. Albers and G. B. Nichols.—p. 260.
Roentgen Examination of Gastrointestinal Tract. M. C. Soaman.—p. 263.
Ulcerative Colitis. E. B. Speir.—p. 266.
Treatment of Ulcerative Colitis. W. L. Voegtlin.—p. 267.
Surgical Aspects of Ulcerative Colitis: Indications for Surgical Intervention and Technic. C. E. MacMahon.—p. 269.
Psychologic Aspects of Ulcerative Colitis. W. Y. Baker.—p. 271.
Present Status of Peptic Ulcer Problem. D. M. Green.—p. 273.
Polyps of Large Intestine. C. P. Schlicke.—p. 276.
Acute Appendicitis After Middle Life. O. F. Lamson.—p. 279.
Enuresis, A Common Sense Treatment. N. W. Clein.—p. 281.

47:335-392 (May) 1948

Trauma to Kidney: Mechanism of Injury, Diagnosis and Management. J. H. Harrison.—p. 337.
Treatment of Bladder Carcinoma by Total Cystectomy. C. D. Goodhope.—p. 341.
Urinary Infections in Presence of Residual Urine. P. A. Rohrer. p. 344.
Physiologic Changes in Presence of Residual Urine. D. Parker.—p. 346.
Differential Diagnosis of Amenorrhea. H. Lisser.—p. 349.
Experiences and Technic in Vaginal Hysterectomy. A. F. Lee.—p. 350.
Inguinal Ectopia of Ovary. F. B. Packard and E. M. Rector.—p. 354.
General Infections of Pregnancy. J. C. Brougher.—p. 356.
Combined Extrauterine and Intrauterine Pregnancy. J. O. Rude.—p. 358.
Prevention of Nasal and Personality Deformities Resulting from Injuries in Childhood. C. Firestone.—p. 359.

Ohio State Medical Journal, Columbus

44:439-560 (May) 1948

Practical Surgical Points in Strabismus. M. P. Motto.—p. 465.
Ménière's Disease. W. C. Thornell.—p. 469.
Severe Allergic Sensitization to an Estrogenic Cream. H. N. Cole Jr., W. L. Marmelzat and A. E. Walker.—p. 472.
Acute Gallbladder. R. M. Zollinger and H. T. Gross.—p. 473.
Treatment of Varicose Veins During Pregnancy by Combined High Saphenous and Segmental Ligations Followed by Injection of Residual Varicosities. P. J. Shank.—p. 477.
Rorschach Test in Clinical Psychiatry. H. S. Evans and Grace M. Collet.—p. 482.
Whence Came You? F. A. Riebel.—p. 487.
Initial Symptoms of Pollenosis at an Advanced Age. McKinley London.—p. 489.

Pennsylvania Medical Journal, Harrisburg

51:729-816 (April) 1948

Practical Considerations in Management of Arthritis. R. H. Freyberg.—p. 729.
Management of Allergic Disease of Respiratory Tract in Children. G. B. Logan.—p. 739.
Philosophy of Medical Service Plan. F. L. Feierabend.—p. 747.
Rhinoplastic Procedures to Establish Normal Physiologic Nasal Function. M. S. Ersner.—p. 749.
Primary Carcinoma of Liver. H. F. Hunt and S. W. Berkheiser.—p. 755.
Trochanteric Fractures of Femur Treated by Internal Fixation. G. Hammond.—p. 759.
Bone Marrow Infusions in Infancy. J. C. Williams and J. Lockhart.—p. 767.
Significance of Hypertension in Pregnancy. L. F. Ritmiller, I. L. Messmore and R. E. Nocodemus.—p. 771.

51:817-944 (May) 1948

Gastric Carcinoma. S. F. Marshall.—p. 841.
The World Medical Association and Its Implications. E. L. Bortz.—p. 848.
A Newspaperman Looks at the Medical Profession. J. F. James.—p. 851.
Reviving the Dormant County Medical Society. A. Laird.—p. 857.
Cataract Extractions Under Intravenous Pentothal Sodium Anesthesia. C. H. Jacobs.—p. 861.
Some Considerations Regarding Treatment of Hemangiomas. R. H. Chamberlain and E. P. Pendergrass.—p. 867.
Mistreatment of Common Skin Diseases. M. H. Cohen.—p. 870.
Management of Premature Labor. H. A. Power.—p. 875.
Immediate Care of Premature Newborn Infant. H. W. Erving.—p. 877.
Social Psychiatry. L. M. A. Maeder.—p. 880.

Public Health Reports, Washington, D. C.

63:593-636 (May 7) 1948

Studies of Fungus Antigens: III. Sensitization of Normal Animals with Skin Test Antigens. A. Howell Jr.—p. 595.
Isolation of Pathogenic Fungi from Experimentally Inoculated Guinea Pigs. A. Howell Jr.—p. 602.

63:637-672 (May 14) 1948

Illness Among Infants, with Comparative Mortality Data. S. D. Collins.—p. 637.

63:673-704 (May 21) 1948

State-Local Grant-In-Aid Formulas. A. L. Chapman.—p. 673.
Changes in Age Selection of Fatal Poliomyelitis. A. G. Gilliam.—p. 677.
Studies of Acute Diarrheal Diseases: Immunization in Shigellosis. A. V. Hardy, Thelma DeCapito and S. P. Halbert.—p. 685.
Sickness Absenteeism Among Industrial Workers, Third and Fourth Quarters of 1947: Trend of Disabling Morbidity, 1938-1947. W. M. Gafafer.—p. 689.
Distribution of Endemic Typhus in Rats in Lavaca County, Texas. J. V. Irons, J. N. Murphy Jr. and D. E. Davis.—p. 692.

Review of Gastroenterology, New York

15:349-438 (May) 1948

Syphilis of Stomach: Report of Case with Gastroscopic Findings and Intragastric Photographs in Color. H. A. Rafsky, M. Weingarten and W. F. Herzig.—p. 359.
Pitfalls in Diagnosis of Jaundiced Patient: Intrahepatic Arrest of Bile Flow. F. Steigmann and H. Popper.—p. 367.
*Abdominal Epilepsy. M. T. Moore.—p. 381.
Studies on Dissolved Mucin (Mucoprotein) of Gastric Juice: I. Preliminary Tests and Rationale for a New Colorimetric Quantitative Method for Determination of Dissolved Gastric Mucin. G. B. J. Glass and L. J. Boyd.—p. 396.

Diagnosis of Jaundice.—According to Steigmann and Popper, one of the main pitfalls in the differential diagnosis of jaundice is presented by primary hepatitis with intrahepatic arrest of bile flow. In these patients, the clay-colored stools, although usually pointing to "surgical" jaundice, are due not to any mechanical obstruction in the extrahepatic bile passages but to some pathologic changes within the liver itself—"medical" jaundice. The absence of bile from the intestine is established by examination of the feces and urine on consecutive days. In a series of 212 patients with jaundice due to hepatitis, 36 (17 per cent) failed to show urobilinogen in their urine or feces for three to forty-one days, with an average of eleven days. This phenomenon was found in all age groups, although it was predominantly encountered in patients between 40 and 50 years of age. The absence of bile from the intestine appears to be somewhat more common in the toxic than in the infectious type of hepatitis. It seems frequently to be encountered in cases of hepatitis following arsenical injections and after ingestion of cinchophen. In cases of cirrhosis complicated by acute damage to the liver, it may be an additional complicating factor. Awareness of this condition and careful and prolonged observation of patients with hepatitis with this phenomenon, by clinical and laboratory means, will ultimately lead to correct diagnosis and management. It is advisable to do an exploratory operation in any patient with prolonged arrest of bile flow in whom the slightest possibility of an extrahepatic obstruction remains. The possible mechanisms for intrahepatic arrest of bile flow are actual obstruction in the region of the canal of Hering in some, and functional changes in the terminal bile ducts in other cases.

Abdominal Epilepsy.—Moore reports 3 cases of abdominal epilepsy with paroxysmal abdominal pain and disturbed motility of the gastrointestinal tract in women aged 50 and 32 and in a boy aged 12 who showed satisfactory response when placed on anticonvulsant therapy. Each of the cases satisfied either all or most of the following criteria necessary to establish the diagnosis of abdominal epilepsy: (1) the patients must be examined by all available methods to rule out intrinsic disease of the pelvic, abdominal and thoracic viscera, morbid involvement of the spinal cord or peripheral nerves and psychosomatic projection mechanisms; (2) historical data regarding the possible existence of cerebral disease or dysfunction should be uncovered; (3) the behavioristic occurrence of the pain should adhere to the pattern of epilepsy; (4) the presence of associated epileptic phenomena, either preceding or during the episodes of abdominal pain, will form corroborative evidence of the nature of the disorder; (5) positive neurologic signs and findings from laboratory studies including cytologic and chemical, roentgenologic studies of the skull and electroencephalographic studies, indicating the existence of a cerebral structural or physiologic disorder, should be in evidence; (6) favorable effects of anticonvulsant drugs on the occurrence of abdominal pain and/or abnormal gastrointestinal motility should be exhibited, and the influence of these drugs on the electroencephalogram should in most instances parallel the clinical results. Absence of abnormal cerebral discharge as observed in the electroencephalogram may be encountered in patients with abdominal epilepsy as in epilepsy of all types.

South Carolina Medical Assn. Journal, Florence

44:113-154 (April) 1948

Acute Porphyria. R. R. Coleman.—p. 117.
Carcinoma of Terminal Ileum: Case Study. K. M. Lippert, H. Potasky and L. E. Nolan.—p. 123.
Mental Hygiene Clinic in Spartanburg. J. M. Pratt.—p. 127.

Southern Medical Journal, Birmingham, Ala.

41:389-486 (May) 1948. **Partial Index**

*Multiple Calcinosis Associated with Hypervitaminosis D.: Report of Case. G. McLean and L. Lebo.—p. 389.
Important Factors in Surgical Removal of Ureteral Calculi. H. W. McKay, H. H. Baird and K. M. Lynch.—p. 394.
Factors Influencing Healing of Anorectal Surgical Wounds. J. McGivney.—p. 401.
*Venereal Granulomas: Comparative Study of These Diseases in Florida. W. W. Wilson.—p. 412.
Use of Interfacet Vitallium Screws in Hibbs Spine Fusion. L. D. Baker and W. A. Hoyt Jr.—p. 419.
Temporal Arteritis with Associated Optic Atrophy. W. B. Anderson, W. M. Nicholson and Lalla Iverson.—p. 426.
Principles of Therapy in Allergic Diseases. W. C. Spain.—p. 439.
What Can We Expect from Electro-Sleep (Electro-Shock) Treatment? C. S. Holbrook.—p. 444.
Complete Industrial Health Service at Atomic Energy Laboratory. Jean S. Felton.—p. 449.
Importance of Physical Medicine Rehabilitation as Demonstrated by Experience of Veterans Administration. A. R. Dawson and A. B. C. Knudson.—p. 455.
Pseudomonas (Pyocyaneus) Infection of Gastro-Intestinal Tract in Infants and Children. A. J. Schaffer and Ella H. Oppenheimer.—p. 460.
Spinal Anesthesia in Obstetrics. M. C. Beck and R. C. Ball.—p. 467.
Cesarean Section: Results in 533 Consecutive Operations. C. Bachman.—p. 473.
Prevention of Heat Prostration by Use of Vitamin C. W. L. Weaver.—p. 479.

Multiple Calcinosis with Hypervitaminosis D.—McLean and Lebo review the history of a man, aged 56, who was first seen by them in April 1945, when he complained of tiredness, loss of weight, lack of concentration, urinary frequency, insomnia, and pain in the neck, shoulders, knees, ankles and feet. He had been treated for hypothyroidism, prostatitis and arthritis. He had taken six capsules daily for the previous two and a half years, or a total of 150,000 international units of vitamin D

and 180,000 units of vitamin A daily. One month before, he had noticed a lump appearing in his right gluteal region, and about the same time painful swellings of his left ring finger, thumb and wrist. Incision into the right gluteal region exposed multilocular cysts which contained a chalky material. The cyst on the left ring finger was also incised and the same type of material was obtained. The presence of calcium was ascertained. Withdrawal of vitamin D was followed by disappearance of symptoms. The authors feel that this is a case of renal insufficiency, anemia and metastatic calcinosis caused by excessive vitamin D therapy. If severe toxic manifestations of vitamin D poisoning are to be avoided, the patients must be subjected to closer observations, periodic laboratory and roentgen examinations and to questions as to whether they are taking vitamin therapy, especially those patients having an unexplainable renal insufficiency, anemia, or calcific deposits in the blood vessels or soft tissues.

Venereal Granulomas.—Wilson lists the total number of cases of chancroid, granuloma inguinale and lymphogranuloma venereum reported to the Florida State Board of Health from January 1942 to August 1947. Florida had 12.4 per cent of the cases of granuloma inguinale reported in the entire country. Laboratory studies and intradermal tests have their limitations in the diagnosis of diseases of this group, but they play an important part in the differential diagnosis. Penicillin has no specific antibiotic action on the etiologic agents in these three diseases. Streptomycin is the most encouraging form of therapy for the rapid healing of patients with granuloma inguinale; this method of treatment has been successful when other methods have failed. Although streptomycin is expensive, the rapid healing it produces and the fact that it aids in the control of this disease seems to justify the expenditure. Sulfathiazole was the drug of choice in the medical treatment of chancroid and lymphogranuloma venereum.

Southern Surgeon, Atlanta, Ga.

16:289-350 (May) 1948

Residual Stones in Cystic Duct Following Cholecystectomy. A. E. Grimes.—p. 289.
Acute Abdomen. C. N. Carraway.—p. 294.
Fractures of Femur: Neck and Trochanteric Region. J. T. Ellis, S. W. Windham and S. G. Latiolais.—p. 309.
Propylthiouracil in Treatment of Goiter. J. G. Dees.—p. 323.
Surgical Treatment of Hypertension. J. E. Thompson, M. H. Harris and W. C. Dine.—p. 326.
Treatment of Anuria by Peritoneal Irrigation. W. H. Cave.—p. 338.
Masquerading Hyperthyroid Patient. S. J. Campbell and R. C. Green. —p. 342.
Controversial Problems in Surgical Treatment of Cancer of Rectum I. Abell, B. T. Beasley and others.—p. 348.

Surgery, St. Louis

23:735-866 (May) 1948

Treatment of Short Stricture of Esophagus by Partial Esophagectomy and End-to-End Esophageal Reconstruction. R. E. Gross.—p. 735.
Leiomyoma of Esophagus and Cardia of Stomach. R. A. Kenworthy and C. Stuart Welch.—p. 745.
An In Vivo Method for Evaluation of Detergents and Germicides. C. A. Hufnagel, C. W. Walter and R. W. Howard.—p. 753.
Choledochotomy. R. W. Buxton and L. B. Burk.—p. 760.
*Myotonia Acquisita Due to Chronic Calculous Cholecystitis and Cured by Cholecystectomy. D. Puppel and Edith Kline.—p. 768.
*Herpes Zoster and Surgical Abdomen. L. H. Bosher Jr. and C. Williams Jr.—p. 773.
Mesenteric Thrombosis. J. E. McClenahan and B. Fisher.—p. 778.
Observations on an Absorbable Powder to Replace Talc. E. L. MacQuiddy and J. P. Tollman.—p. 786.
Magnuson-Stack Procedure for Recurrent Dislocations of Shoulder. N. J. Giannestras.—p. 794.
Plaster Traction Splint for Compound Comminuted Fractures of Tibia and Fibula. M. R. Urist, L. Ries and T. B. Quigley.—p. 801.
Subcutaneous Rupture of Brachioradialis Muscle. A. T. Hamilton. —p. 806.
Four Metachronous Malignant Lesions of Colon: Unusual Case. M. Edwards.—p. 808.
Benign Lymphoma of Rectum. Irene Y. Li.—p. 814.
Gastrostomy: Statistical Review of 199 Cases. D. R. Cooper and R. W. Buxton.—p. 821.
Improved Drain for Peritoneal Lavage. S. S. Rosenak and G. D. Oppenheimer.—p. 832.

Myotonia Acquisita Cured by Cholecystectomy.—According to Puppel and Kline myotonia acquisita is a rare muscular disorder characterized by increased muscular irritability and contractility associated with diminution in the power of relaxation. It constitutes a syndrome which includes the myotonic disorder of movement with stiffness, tension and spasm in the voluntary muscles when movements are initiated, the myotonic reaction with normal mechanical and electrical excitability of the motor nerves, but an increased mechanical and electrical excitability of the muscles, and muscular hypertrophy. The acquired form (myotonia acquisita or Talma's disease) has been differentiated from the congenital form (myotonia congenita or Thomsen's disease) although these may be manifestations of the same pathologic process, which, however, is not fully understood. The acquired form has been described after trauma, dysentery, gastroenteritis, alcoholism, lead poisoning, tuberculosis, and typhoid. Although the disease tends to improve spontaneously, search for the causal factor may be advisable in order to reduce the duration and the severity of the process. The authors present a detailed history of a woman in whom myotonia apparently followed chronic calculous cholecystitis with an associated chronic hepatitis and was cured after cholecystectomy, choledochostomy and adequate treatment of the hepatitis.

Herpes Zoster and Abdominal Symptoms.—Bosher and Williams say that, although investigators have pointed out that herpes zoster may mimic intra-abdominal disorders, the close simulation of conditions requiring surgical intervention is not appreciated. The authors report the case of a 15 year old boy who was admitted to the hospital with a presumptive diagnosis of perinephric abscess in which the diagnosis of segmental neuralgia seemed justified. There was tenderness in the left lower quadrant, flank and costovertebral angle. The tenderness did not increase on deep palpation. It was still present on examination with the abdominal muscles tensed, thus indicating that most of the pain at least was parietal (positive Carnett's sign). After an intercostal nerve block in the region of the tenth and eleventh thoracic nerves posteriorly, the pain and hyperesthesia disappeared. The authors report 2 other cases simulating surgical disease in which there was evidence of herpes zoster. In the first of these, the additional diagnosis of appendicitis was made; a posterior intercostal nerve block would have permitted more accurate evaluation of the apparent deep evaluation of the apparent deep tenderness. The application of Carnett's test, that is, palpation with the abdominal musculature tense, would probably have suggested that the pain and tenderness were predominantly parietal. In the second case, the long interval of ten days between the onset of symptoms and the appearance of the rash postponed the correct diagnosis. The authors stress that Carnett's test is a useful adjuvant in the examination of a patient with abdominal pain.

Texas State Journal of Medicine, Fort Worth

43:66 (May) 1948

Surgery of Major Blood Vessels. H. D. Adams.—p. 10.
Important Considerations in Diagnosis and Treatment of Peripheral Vascular Disease. H. E. Nelson.—p. 15.
Treatment of Pulmonary Embolism by Ligation of Superficial Femoral Veins; Report of 7 Cases. H. N. Leopold.—p. 18.
Cardiovascular Syphilis. R. H. Kampmeier.—p. 23.
Symptoms of Coronary Artery Disease Masquerading as Gastro-Intestinal Symptoms. R. W. Rissler.—p. 28.
Carotid Sinus Syndrome: Its Importance in Clinical Medicine. R. L. Cope and V. C. Baird.—p. 30.
Uses and Abuses of Coagulation and Bleeding Time Preceding Tonsillectomy. W. L. Shepeard.—p. 35.
Epistaxis. B. P. Woodson.—p. 38.
Special Diagnostic Procedures in Cardiac Evaluation. C. F. Shaffer. —p. 40.
Office Procedure in Diagnosis of Squint. A. E. Meisenbach Jr.—p. 43.
Management of Intra-Ocular Foreign Bodies. B. B. Hutchinson.—p. 48.

West Virginia Medical Journal, Charleston

44:97-140 (May) 1948

Venous Thrombosis of Lower Extremities with Particular Reference to Treatment. J. D. German.—p. 97.
Present Status of Ureterointestinal Anastomosis: Case Report. A. J. Oliker.—p. 101.
Treatment of Graves' Disease. K. Nelson.—p. 107.

44:141-176 (June) 1948

West Virginia is Ready for a Four Year Medical School. T. Bess. —p. 141.
Cardiac Changes in Arteriovenous Fistula: Case Report. B. Bradford Jr. and A. J. Beatty.—p. 149.
Practical Aspects of Surgical Care. R. Zollinger and C. Artz.—p. 151.
Urinary Tract Infections. J. W. Merricks.—p. 157.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

60:121-158 (April) 1948

*Vitamin D_2 in Treatment of Cutaneous Tuberculosis. J. Charpy.—p. 121.

Vitamin D in Treatment of Cutaneous Tuberculosis. G. B. Dowling.—p. 127.

Vitamin D Therapy in Cutaneous Tuberculosis. S. Lomholt.—p. 132.

Leprosy in British Nationals. S. Gold.—p. 139.

Vitamin D_2 in Cutaneous Tuberculosis.—The principle of the treatment in which Charpy of Dijon, France, has been interested for the past seven years consists in administering chemically pure vitamin D_2 by mouth in alcoholic solution, in single doses of 15 mg. (600,000 international units), repeated from twice to once a week during many consecutive months. The author reviews personal experience during six years in regard to 150 cases of tuberculous lupus followed from beginning to end and about 60 other cases followed periodically. Vitamin D_2 therapy has changed the usual prognosis of lupus vulgaris. In the favorable cases the therapy influences the inflammatory reaction in the skin. The tuberculous infiltrations, the lupomas, are the most resistant elements. They become paler, but it takes weeks or even months before they disintegrate, separate and finally disappear. It is exceptional to be obliged to supplement the internal treatment by local destruction of residual lupomas. Excellent results are obtained in ulcerated lupus; a little slower in the tumid forms and in the edematous and congestive type; slower still in the erythematonodular lupus ruber planus. Lesions in the mucous membrane disappear rapidly. Adenitis and lymphangitis disappear for the most part during treatment. It is sometimes useful to puncture "cold" abscesses. The therapeutic effect should always be detectable from the beginning of the treatment and should become obvious by the fifteenth day. Should there be no result at that time, lack of absorption, biliary insufficiency, inadequate tissue permeability through an excess of sodium chloride, or the coexistence of syphilis must be considered as factors that may be responsible for the failure of the treatment. Skeptics, although conceding amelioration of lupus, have questioned actual cures, but the author insists that he has seen many patients in whom cure has persisted for three to five years.

British Journal of Radiology, London

21:157-210 (April) 1948. **Partial Index**

Ossifying Hematomata and Other Simple Lesions Mistaken for Sarcomata. J. F. Brailsford.—p. 157.

Significance of Certain Measurements of Skull in Diagnosis of Basilar Impression. M. McGregor.—p. 171.

Accuracy in Radon Work. H. C. Webster.—p. 186.

Presentation and Analysis of Results of Radiotherapy. J. W. Boag.—p. 189.

British Medical Journal, London

1:771-818 (April 24) 1948

Folic Acid. J. F. Wilkinson.—p. 771.

Acute Intussusception in Childhood. B. Morrison and D. Court.—p. 776.

Unusual Case of Adrenal Carcinoma with Note on Application of New Color Test. L. R. Broster and Jocelyn Patterson.—p. 781.

*Adrenal Feminism Due to Carcinoma of Adrenal Cortex: Case Report and Review of Literature. C. N. Armstrong and J. Simpson.—p. 782.

Idiosyncrasy to d-Tubocurarine Chloride. T. C. Gray and J. Halton.—p. 784.

Feminism Due to Carcinoma of Adrenal Cortex.—Armstrong and Simpson review 8 previously reported cases of feminism due to carcinoma of the adrenal cortex and describe a case of their own in a policeman aged 40. In this case laparotomy disclosed a large adherent and necrotic tumor above the left kidney. Because of the vascularity of the tumor mass, its size and extensive adhesions, no attempt was made to remove it. Subsequently the patient deteriorated rapidly; he became emaciated, jaundiced and ascitic, and his liver became enlarged and nodular. Death occurred some eleven months from the onset of his symptoms. There was terminal hematuria. Acquired feminism due to carcinoma of the adrenal cortex causes a well defined syndrome of gynecomastia, abdominal tumor, atrophy of the external genitalia and loss of libido and potency. The condition is rapidly fatal, especially in younger patients. Biochemically there are a moderate excess of urinary androgens and a gross excess of estrogens. A most striking feature is the invariable presence of a palpable abdominal tumor. The possibility that feminism might be due to hyperplasia of the adrenal cortex has been suggested by Broster and Vines, who have clearly shown that virilism can be due to hyperplasia of the adrenal cortex as well as to carcinoma or adenoma. They consider, that, similarly, feminism may be due to hyperplasia of the adrenal cortex.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

55:125-260 (April) 1948

Relief of Severe Stress Incontinence: Technic and Anatomy of Two Suprapubic Fascial Operations. C. McIntosh Marshall.—p. 126.

*Virilizing Tumors of Ovary with Report of Case Associated with Pregnancy. W. N. Searle, M. Haines and J. K. Baker.—p. 135.

Calcium and Phosphorus Metabolism in Pregnancy: Survey Under War and Post-War Conditions: V. Calcium and Phosphorus Balances and Labor Findings. E. Obermer.—p. 142.

Hemoglobin Values in Pregnant Women. A. Sadovsky, W. Koch, R. Toaff and D. Kaplan.—p. 152.

Fibromyoma of Fallopian Tube. J. A. Chalmers.—p. 155.

Investigations Into the Determination of Pregnanediol According to Guterman Method. S. Kullander.—p. 159.

Facts and Fantasy in Study of Female Infertility. J. Stallworthy.—p. 171.

Heart Disease in Pregnancy. D. J. MacRae.—p. 184.

Virilizing Tumors of the Ovary.—Searle and his associates report the case of a woman, aged 33, who showed signs of virilism during pregnancy, particularly change in voice and hirsuties. These changes had become especially noticeable after twenty-four weeks of gestation. The patient delivered a normal child. Some weeks after delivery, the abdomen was opened and a cystic mass was found lying anteriorly to the right broad ligament. A long pedicle had evidently allowed considerable "wandering," and the cyst had finally "jumped" the broad ligament. The cyst was excised. The authors believe that this is the only reported case of an adrenal-like ovarian tumor appearing and causing virilism during pregnancy. Most of the signs of virilism have retrogressed notably since the removal of the tumor. The change in voice, however, remains more or less unaltered. This results from irreversible structural changes in the vocal cords. The ovarian tumor falls into the adrenal-like group. There is no evidence to assess it as a true arrhenoblastoma.

Journal of Physiology, Cambridge

107:129-244 (March) 1948. **Partial Index**

Distribution of Reducing Substances Between Intra-Ocular Fluids and Blood Plasma, and Kinetics of Penetration of Various Sugars Into These Fluids. H. Davson and W. S. Duke-Elder.—p. 141.

Phosphate Clearances in Infants and Adults. R. F. A. Dean and R. A. McCance.—p. 182.

Directional and Spectral Sensitivities of Retinal Rods to Adapting Fields of Different Wave-Lengths. F. Flamant and W. S. Stiles.—p. 187.

Sulfanilamide Inhibition of Carbonic Anhydrase in Whole Blood. D. J. Anderson and L. C. Thompson.—p. 203.

Secretion of Adrenaline from Perfused Suprarenal Gland. Edith Bülbring, J. H. Burn and F. J. De Elio.—p. 222.

Effect of Ulnar Nerve Block on Blood Flow in Reflexly Vasodilated Digit. W. M. Arnott and J. M. Macfie.—p. 233.

Ascorbic Acid in Adrenal Blood. Marthe Vogt.—p. 239.

Journal of Tropical Medicine and Hygiene, London

51:45-66 (March) 1948

Studies in Tropical Ulcer: I. Origin of Epidemic. K. Hare.—p. 47.

Further Observations on Macroscopic Diagnosis of Urinary Schistosomiasis. C. V. Meeser, W. F. Ross and D. M. Blair.—p. 54.

Isolation of Cholera Vibrio. M. A. Gohar.—p. 59.

Practitioner, London

160:339-418 (May) 1948. **Partial Index**

Atopic and Allergic Disturbances of Skin. R. M. B. Mackenna.—p. 339.

Urticaria: Detection of Ingested Allergens: The Single Food Additive Diet. B. H. Winston and R. L. Sutton.—p. 347.

Some Common Industrial Diseases of Skin. P. B. Mumford.—p. 353.

Fungus Infections of Hands and Feet. P. D. C. Kinmont.—p. 359.

Present Status of Sex Hormones in Dermatology. D. I. Williams.—p. 367.

Cosmetics and Care of Skin. G. Hodgson.—p. 373.

Present Indications for Sulfonamides in Venereal Diseases. R. R. Wilcox.—p. 380.

Hospital, Rio de Janeiro

33:505-660 (April) 1948. Partial Index

*Myocardial Lesions in Hyperthyroidism. U. Lemos Torres.—p. 525.
*New Treatment of Barbituric Coma. A. Louzada.—p. 611.

Myocardial Lesions in Hyperthyroidism.—Lemos Torres found, at necropsy on 3 patients who died from congestive cardiac insufficiency and toxic crisis after thyroidectomy for toxic goiter, a serous inflammation of the myocardium in the first patient, which progressed to a fibrosis in the second patient and later to fibroblastic myocarditis, as seen in the third patient. Progressive serous inflammation and the consequent fibroblastic myocarditis are typical of hyperthyroidism.

New Treatment of Barbituric Coma.—Louzada regards picrotoxin as the treatment of choice of barbituric coma. Good results in 2 grave cases are reported from intravenous administration of the drug. The treatment was begun ten hours after ingestion of 46 tablets of 0.1 mg. of "seconal sodium" each. Picrotoxin was given in doses of 21 mg. during the first five minutes, 45 mg. ten minutes later and 30 mg. every hour for eight consecutive hours, followed by three more injections, in doses of 15 mg. each, every three hours up to a total amount of 585 mg. for the whole treatment, which lasted thirty-five hours. The patient should be given intravenous injections of dextrose solution or of sodium chloride solution and of 15 cc. of nikethamide, 10 mg. of adrenal cortex extract, 100 cc. of sodium bicarbonate solution and inhalations of oxygen.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

92:825-896 (March 20) 1948. Partial Index

Tuberculosis After Treatment with Streptomycin. M. Straub and H. E. Schornagel.—p. 832.
Course of Tuberculous Meningitis Under Influence of Streptomycin. A. Verjaal.—p. 841.

Tuberculosis After Treatment with Streptomycin.—Straub and Schornagel describe manifestations of recovery in 4 patients with tuberculous meningitis who were treated with streptomycin, but who died in spite of the treatment. Streptomycin apparently can cure the acute exudative dissemination of tuberculosis before this has assumed the specific histologic character. This is proved by the leptomeningeal changes, the tuberculous primary focus and the acute miliary tubercle. Streptomycin has no distinct influence on productive tuberculous changes, not even on subacute miliary dissemination. These, however, are kept in check by the body itself. Streptomycin, by curing acute exacerbations, gives a chance to the natural defensive power of the body to overcome the disease.

Nordisk Medicin, Stockholm

37:397-458 (Feb. 27) 1948. Partial Index

Hemorrhages During and After Placental Stage of Labor, Their Frequency nad Prevention. H. Sauramo.—p. 399.
Interstitial Pregnancy. N. Clemetsen.—p. 403.
*Some Virus Diseases During Pregnancy and Their Effect on Fetus. H. Grönvall and P. Selander.—p. 409.
*Rubella During Pregnancy and Congenital Defects in Child. M. Zewi.—p. 416.
Full Term Pregnancy with Syncopal Attacks in Dorsal Position. N. Clemetsen.—p. 422.

Virus Diseases and Their Effect on Fetus.—Grönvall and Selander's investigations show that maternal German measles, mumps, acute hepatitis and acute anterior poliomyelitis can be fraught with danger for the fetus. German measles in pregnancy has been less dangerous for the fetus in Sweden than in Australia.

Rubella During Pregnancy and Congenital Defects in Child.—In Zewi's 2 cases from Finland in infants whose mothers had German measles in the first and second months of pregnancy, respectively, there were bilateral congenital cataracts, with microphthalmia in one; in the other, bilateral congenital hydrophthalmus; in both, congenital heart defect. The weight at birth was low; the infants had difficulty in taking nourishment, and their physical and mental development was retarded.

37:459-514 (March 5) 1948. Partial Index

*Penicillin Treatment in Acute Osteomyelitis: Primary Results. E. Eliassen.—p. 466.
*Late Results After Sulfonamide Treatment in Purulent Meningitis. M. F. Hauge.—p. 469.
Thrombocytopenia After Quinidine Medication: Tetany and Myocardial Injury. J. Burstein and B. A. Lamberg.—p. 473.
*Curare in Treatment of Poliomyelitis. N. Normann.—p. 476.
Prostigmine in Acute Porphyria. R. Gordin.—p. 480.
Circulatory Disturbances After Gynergen Treatment. A. Hjertaas.—p. 481.

Penicillin Treatment in Acute Osteomyelitis.—Eliassen gives single massive doses of penicillin (100,000 to 200,000 units) twice a day till the acute stage is past and the patient is afebrile. Roentgenologic examinations afford guidance for the continued treatment. The treatment should be started as early as possible, even on suspected diagnosis of acute osteomyelitis. The essential factor in treatment of this disease with penicillin is believed to be sufficiently long duration of the treatment. In 7 of the 8 cases in which treatment was given during the last year the process seems to have been completely arrested and reparation to be in progress; in 1 case extensive sequestration and fistula formation occurred.

Late Results After Sulfonamide Treatment in Purulent Meningitis.—Of 108 patients with the disease treated with sulfonamide drugs by the mouth and/or with parenteral injection, 27 died. On follow-up of the surviving 81 patients from one half to eight years after discharge, Hauge found permanent organic defects in 10 and permanent psychoneurasthenic defects in 28; of the 66 patients with meningococcic meningitis 7 had permanent organic defects and 16 permanent psychoneurasthenic defects. Sulfonamide treatment of purulent meningitis has not reduced the percentage of permanent and grave defects or milder and transient defects parallel with the mortality, and the late prognosis must be viewed with reservation. It is probable that the more promptly the treatment is started the greater the chance of avoiding defects.

Curare Treatment of Poliomyelitis.—Normann says that curare, tried in 12 cases of poliomyelitis in the acute stage and in 6 in a later stage, was of no definite value in the acute phase but gave good results in 3 of the 4 cases with beginning contractures. Side effects in some instances indicated termination of the treatment. The dosage should be individualized because of the danger of overdosage, as in cases with involvement of the respiratory tract. No conclusion could be drawn as to the efficacy of curare in combination with more radical physical therapy.

37:515-566 (March 12) 1948

Genesis of Renal Hypertension. E. Braun-Ménendez.—p. 515.
Influence of Diet on Renal Function Measured by Inulin and Diodrast Clearance. H. O. Bang and A. Levin Nielsen.—p. 518.
*Treatment of Vesical Tumors. J. P. Strömbeck.—p. 520.
Venereal Disease Among Norwegian Soldiers. A. Strøm and K. Grette.—p. 522.
Asthma in Norway. Statistics on Occurrence and Significance. O. Clausen.—p. 525.
Rash in Mumps. Report from Practice. A. Perdrup.—p. 530.

Treatment of Vesical Tumors.—On the basis of 183 patients treated from 1940 to 1947, one third of whom had benign papillomas, one third malignant papillomas and one third cancer without early papillomatous stage, Strömbeck proposes the following plan: (1) in papillomas of benign type, if small and solitary, transurethral electrocoagulation; if larger and solitary, open electroexcision, possibly with implantation of radium needles, and in papillomatosis, extirpation of the bladder; (2) in papillomas of malignant type, if solitary, electroexcision with implantation of radium needles, and secondary extirpation of the bladder in recurrence; if larger and multiple, primary extirpation of the bladder; (3) in cancer, total extirpation of the bladder, and where this is contraindicated, resection or electroexcision with implantation of radium needles, with care not to make resection or excision too small because of reliance on the radium adjuvant; (4) possible preoperative and postoperative roentgen treatment, and (5) regular control of patients treated without cystectomy so that more effective methods can be employed early in case of possible recurrence.

Book Notices

Cancer: A Handbook for Dentists. Prepared by the Tumor Committee of the Connecticut State Dental Society. Cloth. Pp. 52, with 63 illustrations. Connecticut State Department of Health, Hartford, Conn., 1948.

Connecticut is among the best organized of all of the states in its approach to the problem of cancer. The attack on cancer must be total. Every one of the healing professions is concerned in the earliest possible detection of the symptoms of this disease. The handbook here reviewed is a product of a special committee and is circulated through the Connecticut State Department of Health and the Connecticut State Dental Association. It is magnificently illustrated with black and white and colored illustrations which portray graphically the conditions for which the dentist should be continually observant.

A Research in Marriage. By G. V. Hamilton, M.D. Cloth. Price, $5. Pp. 571. Lear Publishers, 105 E. 15th St., New York 3, 1948.

This is a study on the sexual and a few other aspects of marriage based on a survey of one hundred couples. It is like the Kinsey Report in some ways but unlike it in others. The numbers are much smaller than those on which Kinsey reports. The investigation was based on cards of questions, each subject being examined separately in the private consulting room of the author. Questions were not asked orally, but were presented on the typed cards, of which forty-seven were used for each woman and forty-three for each man. The cards were passed to each subject and the answers were recorded together with notes on significant behavior reactions on the part of the subjects. The results are presented in tabular and narrative form. The author is guarded in his interpretation and conclusions.

The Practitioners' Card Index Guide to Treatment. Boxed. Devereaux (Medical) Publications Limited, 36-37 Malden Lane, Strand, London, W. C. 2, [n. d.].

This is an attempt to present the new and practical methods of therapeutics in the form of an alphabetic card index. Technics, dosage and methodology of treatment with the newer drugs are given in summary form, and many of the cards carry ready references to recent literature for more details. It is the stated intention of the authors to evolve a system that shall become increasingly comprehensive. For this purpose constructive criticism of subscribers has been requested. When fully developed, the card index guide should offer a useful and ready reference for the busy practitioner, particularly if it is kept up to date by frequent review of the newer developments in treatment.

No Retreat from Reason and Other Essays. By Alfred E. Cohn. Cloth. Price, $3.50. Pp. 279. Harcourt, Brace & Co., 383 Madison Ave., New York 17, 1948.

Here are a variety of essays which the author has written over the years. Most interesting are his biographic studies of John Wyckoff and Simon Flexner. In these essays the author reveals himself as a philosopher with an intimate knowledge of art, music and letters. The essays are stimulating, in many instances lightened with wit and humor, and epigrams worthy of quotation. The essay called "On Retiring" is a somewhat cynical comment on an automatic retiring age, quoting great numbers of men who accomplished intellectual marvels beyond the age of 60.

Bases del control sobre la verruga. Por el Dr. Guillermo Gorbitz. Prólogo Dr. Sergio Bernales. Paper. Pp. 55, with 6 illustrations. Corporación peruana del santa, Servicio médico, Lima, Peru, 1947.

This comprises a survey of the epidemiologic problem of bartonellosis (verruga peruana) in Peru, including historical considerations, geographic distribution, vectors and factors important in its control. The importance and usefulness of D.D.T. (4,4'-dichlorodiphenyltrichlorothene) in the control of this disease so far is emphasized and the promise that this drug brings for future more complete control of the disease in Peru is discussed in detail. Several excellent plates, charts, and other illustrative material are included.

An Educational Philosophy for Exceptional Children. Proceedings of the Spring Conference on Education and the Exceptional Child of the Child Research Clinic of The Woods Schools, A Private School for Exceptional Children, Langhorne, Pa., May, 1947. Paper. Pp. 53. Child Research Clinic, The Woods Schools, Langhorne, Pa., 1947.

This brochure contains papers delivered in a symposium at the Woods School in May 1947. Similar conferences and institutes have been conducted at this institution on subjects dealing with the education of the exceptional child each spring and autumn since 1935. The introductory remarks are by Dr. George S. Stevenson, Medical Director, National Committee for Mental Hygiene. The following papers are included: "Theories of Culture and the Deviant," Morris Edward Opler, Ph.D.; "Education as a Factor in Personal Adjustment," Lawson G. Lowrey, M.D.; "Today's Changing Educational Scene," W. Carson Ryan, Ph.D.; "The Importance of Pattern Movements in the Rehabilitation of Cerebral Palsy Patients," Temple Fay, M.D.; "Communication as an Essential Area of Learning," Emmett Albert Betts, Ph.D., and "Modern Woman and the Harvard Report," O. Hobart Mowrer, Ph.D.

While each speaker dealt with the problem in relation to his own field, all were concerned with the role of education in aiding the individual to develop his potentialities fully. This booklet will be of interest to all physicians whose work touches on the educational and adjustment problems of the exceptional child.

The Biological Standardization of the Vitamins. By Katharine H. Coward, D.Sc., Head of the Nutrition Department, Pharmaceutical Society of Great Britain, London. Second edition. Cloth. Price, $5. Pp. 224, with illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1947.

This book is devoted to a detailed description of the methods used for the biologic assay of certain vitamins. Assay procedures for vitamins A, B, C, D and E are given but because of the increasing use of microbiologic and chemical technics, some of these now have only historical value or are useful only under special circumstances. Nearly one fourth of the book is devoted to a consideration of statistical methods applicable to the assays discussed in the first part. This discussion is probably the most valuable portion of the book. Nevertheless, this volume has limited usefulness but may be of interest to those engaged in routine bioassay work.

Physiologic Therapy in Respiratory Diseases. By Alvan L. Barach, M.D., Associate Professor of Clinical Medicine, Columbia College of Physicians and Surgeons, New York. Second edition. Fabrikoid. Price, $9. Pp. 488, with 74 illustrations. J. B. Lippincott Co., 227-231 S. Sixth St., Philadelphia 5, 1948.

The first edition of this valuable book was written in 1944 and titled, "Principles and Practices of Inhalational Therapy." So much new knowledge has been contributed since the first edition was written that this second addition was needed. The subject matter is clearly presented and easy to read. The author correlates the pathologic physiology of each disease entity with the physiologic principles which underlie the treatment of the condition by inhalation therapy and other procedures which have value in the management of respiratory diseases. The book is recommended to any one who desires to know the indications and rationale of the physiologic therapy of the disorders of breathing.

Interesting and Useful Medical Statistics. Edited by William H. Kupper, M.D. Cloth. Price, $6.50. Pp. 528. Wm. C. Brown Co., 915 Main St., Dubuque, Iowa, 1948.

This remarkable book consists of reprintings of hundreds of tabulations of numerical data from American medical publications since about 1935. The tables are arranged alphabetically according to subject, and an index facilitates the reader's search for information. The source of each table is stated, and is generally a readily available recent American publication. If prospective readers will remember that the book ignores all foreign literature and all publications before 1935, deals only with periodic literature, is unsystematic and uncritical, makes no mention of other similar works already published (such as the scholarly "Daten und Tabellen für Mediziner" by Vierordt) and expects the reader to look up the context of the tables for himself, this book can be extremely useful to writers and lecturers.

Old Age: Its Compensations and Rewards. By A. L. Vischer, Dr. Med. Foreword by Lord Amulree, M.D., F.R.C.P. Second edition. Cloth. Price, $3.50. Pp. 200, with 9 illustrations. The Macmillan Co., 60 Fifth Ave., New York 11, 1947.

Since Dr. Vischer has been for more than twenty years director of the Municipal Home for the Aged in Basle, Switzerland, he can speak with real authority on the subject of old age. In this book he covers a great deal of ground.

Part I is devoted to a consideration of senescence as a bodily and mental process. Part II deals with the duration of life, under the headings "The Chronological and Physiological Stages of Life"; "The Centenarians"; "Old Age and Longevity in the Animal World"; "Prolongation of Life and Rejuvenation," and "Maladies of Old Age, and the Care of the Aged."

In Part III—"Society and the Individual; Their Attitude Toward Old Age"—Dr. Vischer discusses old age in other civilizations; the relation between the older and younger generations; the achievements of old age, and, finally, the personal attitude toward old age. This section, particularly the final chapter, is the best part of the book. Evidently Dr. Vischer is expressing his own philosophy when he outlines "the personal attitude toward old age," and he is to be congratulated on having achieved the frame of mind that would enable him to say: "old people who remain intellectually active often wear better physically. . . . The secret of the good life in old age lies in the possibility of bringing the mode of life and the chronological phase into harmony, like a well-broken pair of horses . . . with a correct attitude to youth the old man may even come to realize that intercourse with youth can only bring him profit. . . . The dread of overworking is very seldom justified. . . . We . . . want to prolong not only life, but also achievement."

Diseases of the Chest Described for Students and Practitioners. By Robert Coope, M.D., B.Sc., F.R.C.P., Hon. Physician, Royal Liverpool United Hospital (Liverpool Royal Infirmary). With a foreword by Lord Horder. Second edition. Cloth. Price, $7.50. Pp. 541, with 188 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

The chief revision in this the second edition of this book is in the bronchopulmonary anatomy, which has been brought to conform more closely to the modern American concept emphasizing the bronchopulmonary segments. The book is apparently written primarily for the medical student in the clinical years. Much space is devoted to physiology and to symptoms and physical signs with mechanisms of their production. The discussion of tuberculosis is very good except that streptomycin is not mentioned. The chapter on bronchial carcinoma is excellent, and the drawing illustrating the metastatic sites is especially illuminating. The discussion of fungous diseases is inadequate, and histoplasmosis is not even mentioned. There is a paucity of roentgenograms which is refreshingly at variance with the recent American tendency to make the literature on the chest top-heavy with them. The author endeavors "to set forth how diseases of the chest should be taught." He has produced a book which is excellent for the undergraduate and helpful to those in actual practice. The style is pleasing and, all things considered, the volume is well worth while to any one interested.

Recent Progress in Hormone Research: The Proceedings of the Laurentian Hormone Conference [1946]. Volume II. Edited by Gregory Pincus. Committee on Arrangements: R. W. Bates, R. D. H. Heard and G. Pincus. Cloth. Price, $4. Pp. 427, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10, 1948.

This is the second volume of what promises to be a valuable annual contribution to the literature on endocrinology. Following the pattern established by the first volume, the present book presents the papers and discussions given at the 1946 Laurentian Hormone Conference. The first two reports in the book present a stimulating discussion of the new physical-chemical assay methods for estrogenic hormones. At last it appears likely that quantitative chemical assays may replace laborious and costly biologic determinations of the estrogens, and that the various types of estrogens can be separated and quantitatively determined. The section on pituitary control and activity deals largely with pituitary-adrenal relationships, with the luteinizing hormone and with the hormonal control of lactation. The last-named subject is particularly well presented by W. E. Petersen. Hormone metabolism receives attention in two papers, one by Roy Hertz and the other by Ralph I. Dorfman. Although the papers are confined to estrogens and androgens, considerable light is thrown on the metabolism of other steroids. Hormonal regulation of metabolism is discussed from the standpoint of insulin secretion, relation of thyroid activity to diabetes and the actions of the toxic thioureas. Finally, the clinical aspects of endocrinology are presented in reports dealing with sex hormone deficiencies, adrenal cortical tumors and the genetic and endocrine factors in the growth and development of childhood and adolescence. This volume will be of exceptional value to the steroid chemist and to the experimental and clinical endocrinologist.

The Care and Management of Laboratory Animals: Handbook of the Universities Federation for Animal Welfare. With an Appendix on Statistical Analysis. Edited by Alastair N. Worden, M.A., B.Sc., M.R.C.V.S., Milford Professor and Director of Research in Animal Health, University College of Wales, Aberystwyth. With a foreword by Professor T. Dalling, M.A., M.R.C.V.S., F.R.S.E., Director, Veterinary Laboratory, Ministry of Agriculture and Fisheries, Weybridge, Surrey. Cloth. Price, $8.50. Pp. 368, with 70 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1947.

In addition to presenting in meticulous detail all necessary information regarding proper care of laboratory animals, this volume contains a general chapter, by Major C. W. Hume, M.C., B. Sc., on law and practice in relation to the rights of these important partners in medical research. The discussion contains historical notes and a presentation of basic principles that should be required reading for every laboratory worker, from director to bottle washer. Carrying the subtitle, "Handbook of the Universities Federation for Animal Welfare," the book contains contributions from numerous reliable sources. There is some lack of orderliness in the approach of the various chapters as a result, but this is unimportant. All chapters include details on stock accommodation and equipment, feeding, handling and marking, breeding, anesthesia and species diseases and their control. Sixty-three illustrations, including diagrams and photographs of pens, cages and tanks, add to the practical value of the discussion. There are details on a wide variety of laboratory animals in common use, including the ferret, various rat and mouse species, the vole and the rather recently introduced golden hamster. A special chapter is devoted to pests of the animal house and their control, and another contains notes on care of anthropoids, dogs and cats, horses, shrews, vampire bats, poultry, reptiles and marine forms. In an appendix is presented a comprehensive survey of the elements of statistical analysis by Major Hume, with special sections on biologic assay and planning. The entire section is replete with formulas, charts and tables. The book should provide much aid for laboratory workers everywhere.

When You Marry. By Evelyn Mills Duvall, Secretary, National Council on Family Relations, and Reuben Hill, Associate Professor of Sociology, Iowa State College, Ames, Iowa. Cloth. Price, $3. Pp. 450, with illustrations. Association Press, 347 Madison Ave., New York 17, 1948.

One of the authors of this book is secretary of the National Council on Family Relations; the other is associate professor of sociology in Iowa State College. The preface states that "this book has been written to supply the kind of guidance that is sought and needed 'when you marry.'" The foreword emphasizes the functional approach to teaching marriage and family living, and explains at some length how this is accomplished. The foreword is written by Ernest W. Burgess, of the University of Chicago.

The book is organized into four parts, dealing respectively with "Anticipating Marriage," "What It Means to Be Married," "The Making of a Family" and "Family Life Yesterday, Today, and Tomorrow." On the jacket it is claimed for the book that it covers the gamut of personal relationships from first date to last baby. In general it may be said that this claim is fulfilled.

In part I are chapters dealing with what the partners bring to the marriage with respect to heredity, personality development and other qualities. The second chapter essentially deals with the question: "How do you know it's love?" Subsequent chapters deal with dating, courtship, the meaning of an engagement, who gets married and to whom, marriage

and the facts of life, and morality makes sense. With the aid of amusing cartoons and an informal style, these chapters make easy reading, and they present a sensible philosophy which is neither too radical nor so conservative that youthful readers will be repelled.

In part II are chapters for the information of those just married, including suggestions about the honeymoon and settling down, establishing housekeeping and the major accomplishments of the first year of marriage. Another chapter deals with common conflicts in marriage and some rather surprising but definitely sensible thoughts about productive versus destructive quarreling. Marriage counseling is advocated as a help in many instances. There is a good chapter on money in relation to marriage and one on crises in the family relationships, including financial crises, desertion, infidelity and death. This is logically followed by a chapter on divorce which is unavoidably controversial. Those who adhere to the traditional opposition to divorce which is inherent in the belief of a number of religious groups will condemn the book on the basis of this chapter, which frankly has as its keynote the headline of one of its subsections, "Divorce Not Something to Fear or Condemn." On the other hand, this very attitude may recommend the book to persons of views divergent from those previously mentioned. Immediately following the chapter on divorce is one on what holds a marriage together. Part III has to do with the making of a family, with chapters on where babies come from, illustrated by photographs of the Dickinson models, another chapter on getting ready to be parents, one on what it means to be parents, and one on family life and religious living. This chapter will please or displease readers according to their religious views. Part IV has to do with the orientation of the family in relation to the past, the present and the future.

Subject to the differences of opinion inherent in philosophic and religious points of view, this book can be recommended for physicians to suggest to their patients.

The Baby's First Two Years. By Richard M. Smith, A.B., M.D., Sc.D. Fifth edition. Cloth. Price, $2.75. Pp. 181, with illustrations. Houghton Mifflin Co., 2 Park St., Boston 7, 1948.

The material has been rewritten completely in many sections of this book to conform with recent knowledge concerning the care of infants. It has been an authoritative book for mothers for the past twenty years or more. The volume is divided into three parts. Part 1, "The Care and Feeding of Infants," includes not only the usual chapters, but also one each on "Growth and Development," "Habits and Training" and "Sickness." Part 2, on "Suggestions to Mothers," contains a valuable chapter on "How to Travel with a Baby" and another on "A Typical Day," which summarizes and coordinates much of Part 1. Part 3 concerns itself with "Recipes and Charts." There are 181 pages of easily readable type, an index and 15 photographs ½ to 1 page in size illustrating such things as putting on a diaper and equipment for the bath. This edition is written in an easily understandable, matter of fact style. There is perhaps not as much space given to psychologic phases and discussions as in some other recent "Baby Care" books. Dr. Smith takes a middle of the road attitude regarding daily schedules. He believes that the pendulum may have swung too far in both directions at various times.

I Love My Doctor. By Evelyn Barkins. Cloth. Price, $3. Pp. 238, with illustrations by Alfred S. Plane. Thomas Y. Crowell Co., 432 Fourth Ave., New York 16, 1948.

This author loves *her* doctor, but she does not seem to love the medical profession or the practice of medicine. In the early chapters the doctor is still finishing his internship and the author studying for her degree in law. The story deals with the setting up of an office, the buying of a car, waiting for practice to appear and other events. One is not sure at first whether the primary purpose is to write an experience book on early marriage or one on starting a medical practice. While the author loves her own doctor, she seems to think most other doctors stupid. She jeers at medical meetings in general, tries to keep her husband off hospital staff appointments because she considers them political, and derides the scientific councils of the American Medical Association, of which, incidentally she does not trouble to ascertain the correct names. Just why a doctor's wife should consider it funny to belittle the profession to which her husband belongs is not clear. The preceding book by this author has had a wide sale, and is said to have been hilariously funny. This one is not.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart. Eleventh edition revised by Lambert Rogers, M.Sc., F.R.C.S., F.R.C.S.E., Professor of Surgery, University of Wales. Fabrikold. Price, $6. Pp. 360, with 192 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1947.

This little book, originally written sixty years ago, is probably the oldest textbook of surgical anatomy written in English to remain in current use. Despite its age and many revisions, it still fulfils Treves' conception of a "modern account of the application of anatomy to practice." It divides the body into six regions—head and neck, thorax, upper extremity, lower extremity, abdomen and pelvis, and spine and cord. Each is amply covered from the standpoint of general surgery as well as of the various surgical specialties. Many subjects, such as surgery of the blood vessels, which deals with ligations, abnormalities and collateral circulation, are omitted for the sake of brevity, "since these are fully treated in manuals of general anatomy." The work is easy to read. It is not abundantly illustrated, but the drawings present enhance the value of the text. The survival as well as the appeal of this book to the student, teacher and practitioner, particularly in England, is indicative of its usefulness.

Physical Treatment of Injuries of the Brain and Allied Nervous Disorders. By K. M. Horn, M.C.S.P., in Charge of Physiotherapy Dept., Military Hospital (Head Injuries), Oxford. With a foreword by Air Vice-Marshal Sir Charles P. Symonds, K.B.E., C.B., D.M. Cloth. Price, $4. Pp. 96, with 34 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1947.

This short monograph presents in considerable detail a method of treatment of hemiplegia and other upper motor neuron disorders by means of active exercises. These include methods of teaching walking and rhythmic exercises for coordination with minimal apparatus. To develop functional ability of the upper extremities the most important equipment is three sizes of balls used in exercises and games. Other standard gymnasium equipment is also described and advocated. A few types of occupational therapy procedures are included. The complete problem of rehabilitation of these patients including social and economic adjustment is not fully covered. Physicians and technicians dealing with these problems will find practical information satisfactorily described and illustrated. It is recommended more as a reference textbook, as it does not completely cover the problems in this important field of physical rehabilitation.

Die Röntgendiagnostik der Wirbelsäule und ihre Grundlagen. Von Dr. med. Adolf Liechti, Professor für medizinische Radiologie, Direktor des Röntgeninstitutes der Universität Bern, Bern. Second edition revised by A. Eggli. Paper. Price, Dollar br. 13. Pp. 364, with 234 illustrations. Springer-Verlag OHG, Mölkerbastei 5, Vienna 1, 1948.

This book is written from the point of view of the radiologist. He describes the embryology of the vertebra and the disks, the various stresses and strains to which the back is subjected, and the physiology and static factors of the muscles of the back. He illustrates hemivertebra, butterfly vertebra, spina bifida, gorilla vertebrae and various anomalies and variations. Scheuermann's lesion, Calvé's lesion, and Cushing's lesion, arthritis of all types and infections, osteomyelitis and primary and secondary tumors are discussed. The bibliography, chiefly foreign, occupies 96 pages. This makes the book top heavy.

Control of Pain with Saddle Block and Higher Spinal Anesthesia. Edited by J. B. Walton, M.D., Cloth. Gratis to Physicians. Pp. 52, with illustrations by Frank H. Netter, M.D. Ciba Pharmaceutical Products, Inc., Summit, N. J., 1948.

This monograph describes the technics and gives other pertinent data on saddle block anesthesia (low spinal anesthesia limited more or less to anatomic parts that would be in contact with rider's saddle) and conventional spinal anesthesia for normal and operative obstetric deliveries. The only drug recommended is dibucaine hydrochloride. There are 12 excellent plates in color drawn by Frank H. Netter, M.D. The monograph will interest anesthetists and obstetricians.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

LOSS OF HAIR PIGMENTATION

To the Editor:—What could be the cause of the loss of pigmentation of the eyelashes and eyebrow of the right side over a period of three to four months. This patient is 4 to 5 years of age and somewhat overweight. Present weight is 58½ pounds (26.5 Kg.). What is the possible etiology and treatment in this case?

Darrel L. Evans, M.D., Manhattan, Kan.

ANSWER.—Premature whitening of the eyelashes and eyebrows, not due to locally applied bleaching agents, has been described in association with a number of diseases and injuries. Alopecia areata and vitiligo frequently accompany the disorder, and it has been described as occurring in trigeminal neuralgia, nerve injuries, peripheral neuritis, severe emotional trauma, iridocyclitis, interstitial keratitis, sympathetic ophthalmia, and following painful ocular surgical operations. Theoretically, the loss of pigment is ascribed to rapid penetration of the hair by air, to inhibition of pigment formation in the cortical cells of hair-bearing skin, to a circulatory change causing disturbances in distribution of pigment, to anaphylactic phenomena and to congenital factors.

No treatment is indicated; the affected hairs usually regain their pigment in a few months. Occasionally removal of the white cilia is followed by a growth of normally pigmented hairs. A good review and bibliography of the subject is contained in Hague (Uveitis; Dysacousia; Alopecia; Poliosis and Vitiligo. *Arch. Ophth.* **31**:520, 1944).

TETRACHLORETHYLENE

To the Editor:—Please discuss the toxic effects of perchlorethylene on the liver as compared with carbon tetrachloride and trichlorethylene. What other chemicals does a "silk spotter" come in contact with that might cause damage to the liver? Would it be advisable for a "silk spotter" using perchlorethylene and having evidence of Laennec's cirrhosis of the liver to return to his occupation?

Lieut. (jg) W. H. Spruit, MC, Batavia, N. Y.

ANSWER.—Perchlorethylene (tetrachlorethylene) along with trichlorethylene is much less toxic than carbon tetrachloride. In part this is due to lower vapor pressure and in part to the fact that perchlorethylene in the body decomposes to less active constituents while carbon tetrachloride likely remains intact and at least in exhaled air appears as such. Moreover, perchlorethylene damages the liver to a lesser extent than carbon tetrachloride. Its chief point of action may be on the cardiovascular-renal system and on occasion may be associated with pulmonary edema.

The "silk spotter" in a dry cleaning establishment is the "fancy spotter" doing work more complicated than the "rough spotter." Fancy spotting, in addition to silks, extends to divers synthetic fabrics. The silk spotter's table is likely to present a large array of chemicals calling for skill and experience. Some chemicals highly suited to silk will dissolve the synthetics. This trade is highly individualistic. Every spotter is likely to have a few personal secret concoctions that make him superior to the ordinary spotter. Almost anything may appear on his bench. The number will include carbon tetrachloride, perchlorethylene, chloroform, benzene, naphtha fractions, phenols and creosols, hydrofluoric acid, acetic acid, ammonia water, carbon disulfide, various alcohols, and such.

Spotter's benches are practically never ventilated. They should be. Since as little as a spoonful of carbon tetrachloride may provoke disaster it may be believed that this and other practical exposures readily come about. However, the real problem is not what chemicals appear on the spotting bench but instead how extensive the exposure therefrom and what protection is provided. "Spotters" like galvanizers are prone to alcoholism, there possibly being some "stimulatism" from the chemicals employed. Any persons with Laennec's cirrhosis probably may be more easily involved in further hepatic damage than a wholly normal person. It would appear that the more salutary answer may derive from properly ventilated work booths rather than from removing the spotter involved in some degrees of hepatic damage. Alcoholism should be discouraged. Particularly alcohol accelerates the action of carbon tetrachloride.

BARBITURATES

To the Editor:—What are the relative merits of pentobarbital sodium ("nembutal") and "seconal sodium" as compared with phenobarbital and the specific indications for and dosages of each of these drugs?

S.S. Lasky, M.D., Brooklyn, N. Y.

ANSWER.—Pentobarbital sodium ("nembutal") and "seconal sodium" belong to the group of barbiturates usually classified as "short acting," whereas phenobarbital belongs to the "long acting" group.

Pentobarbital and "seconal" may be used as hypnotics to induce sleep in nervous or excitable patients. The rapid destruction in the body generally assures that the depressant effects will have disappeared at the end of a normal period of sleep (eight hours), and hence the so-called "barbiturate hangover" is usually absent. The hypnotic dose of pentobarbital and "seconal" is about 0.1 Gm. Both drugs may be used for preanesthetic sedation, the dose being 0.1 to 0.2 Gm.

Phenobarbital, because of the presence of the phenyl group has a prolonged action and is used wherever prolonged sedation is required. Hence it is not useful for the treatment of insomnia or as preanesthetic medication. Phenobarbital is chiefly used as a sedative and anticonvulsant in the treatment of epilepsy and has also been proposed as a sedative in circulatory and cardiac disorders. The average dose is 0.1 Gm.; the dose varies from 15 mg. to 0.2 Gm.

JIUJITSU

To the Editor:—Would jiujitsu not represent an ideal sport for self defense and physical training avoiding the dangers and brutalizing effects of boxing?

Leopold J. Schwarz, M.D., Wildwood, N. J.

ANSWER.—Various sources classify the technics of judo or jiujitsu into three divisions or "arts" including throwing (nage-waza), holding down (kataame-waza) and striking (ate-waza).

While judo or jiujitsu means "gentle way" or "gentle art"—first giving way so as to gain eventual victory, its striking, kicking and choking aspects hardly fit the definition.

Among the approved methods of scoring a point and winning a bout are: throwing the opponent flat on his back, holding the opponent down for thirty seconds, choking the opponent until he becomes unconscious or signifies defeat, causing the opponent to give up through the application of torture holds, hitting the opponent in a vulnerable spot.

During the last war, the immediate enemy in the Pacific happened to be the chief exponents of the activity. Interest in judo or jiujitsu in this country naturally became intensified. It is doubtful whether the activity would normally fit into the sport mores of what is now a rather well established American pattern. Further, as a peacetime pursuit, it is difficult to reconcile such activity with the social aims of a democracy.

In time of war, when the individual becomes more or less expendable, the situation is altered. With life or death sometimes dependent on skills of self defense, in hand to hand combat any means to the end becomes acceptable. The technics of judo, however, cannot be mastered in a short training period. Japanese experts spend years learning its intricacies, advancing through several ranks before qualifying for the higher ratings. In this connection it is interesting to note that toward the end of World War II many of our leaders became convinced that the best means of self defense for American youth were to be found in the familiar rough and tumble tactics growing out of American sports, coupled with those disarming and offensive skills that could be taught in a relatively short period of time.

ERYTHROBLASTOSIS

To the Editor:—What is the relation of apparently a cured erythroblastosis fetalis to the subsequent development of spasticity in the child? Please give sources for further information.

Robert E. Hoerner, M.D., Batavia, Ill.

ANSWER.—The relation of erythroblastosis fetalis to cerebral damage is obscure, but it is quite clear statistically that there is an extreme high incidence of infantile jaundice and blood incompatibility among children suffering from mental deficiency, athetosis, spasticity and other cerebral defects of early infancy. The subject has been considered in several recent publications, among which are the following:

Yannet, H., and Lieberman, R.: Central Nervous System Complications Associated with Kernicterus, J.A.M.A. **130**:335-340 Feb. 9, 1946. Neurological Defects and the Rh Factor, Internat. Med. Digest. **40**:35-38 (Jan.) 1946.

TRICHOMONAS VAGINALIS

To the Editor:—What is the latest information on treatment of Trichomonas vaginalis infection? I have 2 patients that I have been unable to relieve. We have used all standard treatments and searched for all points of infection and sources of reinfection.

Sam B. McFarland, M.D., Lebanon, Tenn.

ANSWER.—In nearly all cases of Trichomonas vaginalis infection, relief can be given the patient promptly by many forms of treatment. However, while it is easy to produce a temporary cure it is often difficult to give permanent relief. In refractory cases and in cases in which recurrences are frequent, a diligent search for a source of reinfection must be sought in the cervix, Skene's glands, the bladder and urethra, Bartholin's glands, the rectum and the husband's prepuce and prostate. Of course, if the trichomonads are found in any one of these organs, an effort should be made to get rid of the organisms.

Ray E. Trussell in an excellent book, "Trichomonas Vaginalis and Trichomoniasis," (Springfield, Ill., Charles C Thomas, Publisher, 1947) pointed out that failure to cure vaginal trichomoniasis is suggestive of resistant forms, but he also suggested that (1) rectal, urethral and glandular involvement were overlooked; (2) treatment was inadequate or inappropriate; (3) reinfection occurred, or (4) a drug-resistant strain developed.

Trussell stated: "The final word in the therapy of trichomonas vaginitis is far from having been written. At present the most commonly employed agents included aldarsone, carbarsone, acetarsone, silver picrate, floraquin, lactobacilli, and vioform. There is a current trend to the use of acid creams and jellies with or without the addition of protozoacides other than the acids. Good results have been achieved with most of these in the hands of careful investigators."

In a series of cases in which 98 per cent of the patients were cured, the treatment consisted of drying the vaginal tract and then applying by insufflation 2 to 4 Gm. of a powder containing 20 per cent by weight of finely pulverized mild silver protein ("argyrol"), 40 per cent of kaolin and 40 per cent of beta-lactose.

The patient was instructed to take a nightly douche, containing white vinegar (4 tablespoonfuls to 2 quarts of warm water) followed by insertion high into the vagina of a no. 12 gelatin capsule containing an additional 4 Gm. of the mild silver protein, kaolin and lactose powder. One week's supply of capsules was given, and the patient was asked to return at the end of that time, having taken the only douche (omitting medication) on the night preceding examination.

Patients were instructed to give careful attention to feminine hygiene to prevent reinfection from any of the possible sources. Treatment was not interrupted during the menstrual period.

The number of weeks of treatment given, in the absence of recurrence, was between three and four, and in the presence of one or at most two recurrences, between five and seven.

ENCEPHALOPATHY

To the Editor:—Are there publications on: (a) early differential diagnosis by means of the prothrombin time of embolic, thrombotic or hemorrhagic encephalopathy; (b) therapy of thrombotic encephalopathy by means of anticoagulants such as heparin and "dicumarol"; (c) the relative merit of the anticoagulant method in thrombotic encephalopathy as compared to the method procainization of the ganglion stellatum as described recently by Case de Takats in The Journal (130:659 [March 6] 1948)?

Wladimir G. Ellenberg, M.D., New York.

ANSWER.—The first question is based on the assumption that the prothrombin level of the blood is a measure of the patient's clotting tendency. It is true that the hemorrhagic tendency of jaundice and the state of the blood after "dicumarol" therapy are accompanied by a diminished level of prothrombin in the blood. It has also been observed that increased prothrombin levels, a state of hyperprothrombinemia, can be found in persons shortly after operation or after childbirth. This however, is only true when prothrombin is measured in diluted plasma, and Quick has always criticized these methods as not determining true plasma-prothrombin levels and thus being artefacts.

But even if an increased prothrombin level were a consistent finding in recent intravascular clotting, a diagnosis between cerebral embolus, thrombosis or hemorrhage would not be possible, since all three of these vascular accidents raise the clotting tendency. Thrombosis increases the clotting tendency; embolus of course is a thrombus, broken loose, and hemorrhage is well known to shorten coagulation time; added to this is the state of dehydration in which most of these patients are found within a few hours, and this itself increases the tendency to clotting. The correspondent does not know of any published article which tries to differentiate the three forms of cerebrovascular accident by determinations of prothrombin levels, but on the basis of our present knowledge useful findings cannot be expected.

Question (*b*) refers to the use of anticoagulants in cerebral thrombosis. This is practiced on some services throughout the country but requires the elimination of cerebral hemorrhage from the group under treatment; since anticoagulant therapy per se has been known to produce cerebral hemorrhage, caution is indicated; heparin had better not be employed, and "dicumarol" given in conjunction with 200 mg. of rutin a day to counteract capillary fragility which may develop with the use of "dicumarol." The prothrombin level should not be allowed to drop below 30 per cent of normal in this group of patients.

(*c*) The relative merits of the anticoagulant therapy as compared to the sympathetic block in cases of cerebral thrombosis have not been described. Judging from results obtained in vascular thrombosis of the extremities, both methods can be used simultaneously, since they complement each other and act by different mechanisms; anticoagulants prevent propagation of the thrombus, and sympathetic block relieves the stasis and edema around the cerebral infarct. To answer summarily the three questions of the inquiry: there are no publications available at present. Further information may be obtained by consulting the following authors:

Quick, A. J.: The Hemorrhagic Diseases and the Physiology of Hemostasis, Springfield, Ill., Charles C Thomas, Publisher, 1942.

Brambel, L. E., and Loher, E. F.: Proc. Soc. Exper. Biol. & Med. 53:218, 1943.

de Takats, G.: Heparin Tolerance: A Test of the Clotting Mechanism, Surg., Gynec. & Obst. 77:31 (July) 1943.

Hagedorn, A. B., and Barker, N. W.: Coagulation Time of Blood Heparinized in Vitro; Correlation of Results with Those of the Heparin Tolerance Test. J. Lab. & Clin. Med. 33:1087 (Sept.) 1947.

MALE STERILITY

To the Editor:—What treatment is indicated for a man aged 30 years, otherwise in good health, who is sterile? A fresh specimen of semen shows a large number of well developed spermatozoa, except that they are all immotile.

Robert C. Tevlin, M.D., Mooreland, Okla.

To the Editor:—Is there a hormone that will reactivate spermatozoa that have been in a semidormant state for some time? The patient is 40 years old.

A. E. Goebel, M.D., Montrose, Ill.

ANSWER.—In freshly ejaculated semen the spermatozoa nearly always possess some degree of motility. When examination shows poor motility, or none, the reason is usually a technical fault in collecting or handling the specimen. Materials used in the manufacture of ordinary condoms may kill even the liveliest cells within half an hour. Heat at first stimulates the activity of the spermatozoa, with the end result that their inherent vitality is more quickly exhausted. Cold can immobilize them, thus producing apparent necrospermia though the cells are not necessarily dead.

When initial motility is subnormal or, as happens in rare cases, completely lacking, several possible causes must be considered. Poor spermatogenesis may yield cells so immature or morphologically imperfect that they are incapable of any activity. If the male duct system and its accessory glands do not function properly, spermatozoa may fail to "ripen" in the epididymides or to receive their normal physiologic stimulation from the prostatovesicular secretions. Chronic infection or congestion of the prostate and vesicles may produce such viscosity of the seminal fluid that motility is mechanically impeded.

The first step in differential diagnosis should be the examination of a stained smear of semen with regard to the incidence of poor morphology. Faulty functioning of the epididymides and accessory glands may be indicated by small volume and increased viscosity of the ejaculate, and is further suggested if hormone assays show hypogonadism. Prostatovesiculitis can be diagnosed by the usual methods of studying the expressed secretions.

As a general basis for treatment the patient's health and hygiene receive all necessary attention. If his basal metabolic rate is below plus 10, it should be raised and maintained at that level by the carefully regulated administration of thyroid. More specific therapy will depend on the faults identified in his genital tract. Poor spermatogenesis may respond to gonadotropins, though the results in most cases are disappointing. Small doses of testosterone sometimes improve the functioning of the duct system and its glands; large doses are inadvisable, since they tend to depress the gonadotropic activity of the anterior pituitary. Chronic prostatovesiculitis should be treated by the accepted urologic technics.

PITUITARY DEFICIENCY

To the Editor:—A white woman aged 30 has had her condition diagnosed by competent specialists as a pituitary deficiency. Her major complaints during the period of examination and treatment were facial hirsutism and an abnormally large distribution of fat in t...gs, thighs and hips. She is soon to be married. What are the possibilities of her children inheriting this tendency?

M.D., Arkansas.

ANSWER.—It is impossible to make a diagnosis on the basis of the information provided; it might be impossible with all the information. If this woman 30 years of age is simply fat and hairy and if she has been menstruating, in all probability there is no reason to incriminate the pituitary gland. Most such girls and women respond satisfactorily to a weight-reduction program and local attention for the hirsutism. If this patient is really suffering from a pituitary deficiency, she probably could not become pregnant. In any event, there is no evidence that disturbances of the pituitary gland are hereditary. Every physician has observed obesity and hirsutism as parts of racial and family patterns.

HYPEROSMIA

To the Editor:—What is the best method of dulling the sense of smell? I have a maternity patient with an unusually keen sense of smell, which causes much nausea. If her olfactory organs could be impaired, she would improve.

Eugene Smith, M.D., Waterloo, Ia.

ANSWER.—Although it is a variable entity hyperosmia may be a symptom of hysteria or a psychosis. It may also be an indication of local functional disturbance in the olfactory lobe. The perception of odors is occasionally exaggerated during the early stages of pregnancy. Since nasal pathologic conditions seldom cause hyperosmia, attempts to dull the sense of smell through local medicaments would be inadvisable. During pregnancy psychogenic factors are likely to be strong. Reassuring the patient that she is normal and that the sense of smell will improve are of prime importance. She may be advised to carry on her person a bottle of agreeable perfume to counteract disagreeable odors.

DIABETES INSIPIDUS

To the Editor:—Please give information on use of posterior pituitary extract orally to control the symptoms of diabetes insipidus. Is it as efficacious as when used parenterally?

LaMar J. Hoskamp, M.D., Dalton, Mich.

ANSWER.—Posterior lobe pituitary extract is not effective when given by mouth. It is most effective when given parenterally, and relief of symptoms of diabetes insipidus is obtained in most cases when posterior pituitary or, better still, the antidiuretic principle known as "pitressin" is given subcutaneously. For long-continued effect the intramuscular administration of "pitressin tannate in oil" is desirable.

Good absorption is obtained usually through the nasal mucosa. Many patients with diabetes insipidus respond excellently to the insufflation of posterior lobe pituitary powder, and this, incidentally, is the least expensive form of treatment. Somewhat less effective when applied to the nasal mucosa are ointments and solutions containing pituitary extract.

TRIETHYLENE GLYCOL

To the Editor:—Please furnish information regarding use of triethylene glycol as a preventive of colds and virus infections.

W.B. Ismon, M.D., Soso, Miss.

ANSWER.—The use of triethylene glycol as a preventive for colds and virus infections is still highly experimental. We lack satisfactory evidence that under the conditions of use which would be practicable in a home, office or factory any significant diminution in the incidence of viral infections can be obtained.

Triethylene glycol is manufactured by the Carbon and Carbide Chemicals Corporation and by the Dow Chemical Company.

LIPIODOL

To the Editor:—Is there a substitute for iodized oil ("lipiodol") with which to make bronchogram studies on a patient who has a marked sensitivity to iodine? If so, where can it be procured?

John W. Stacey, M.D., Tucson, Ariz.

ANSWER.—Unfortunately, there is no satisfactory substitute for iodized oil in bronchography. Experimentally, compounds containing bromine have been tried, but they are too irritating and fail to cast a satisfactory shadow.

COBRA VENOM

To the Editor:—What is the consensus relative to the use of "cobra venomin" in intractable pain in cancer? A patient is using more narcotics with less relief. Prognosis is that she will live for another year or more.

G. N. Grove, M.D., Elgin, Ill.

ANSWER.—The pharmacology and the therapeutic value of preparations of cobra venom (naja) have been described in the following references.

The consensus is that cobra venom is useful in relieving severe chronic and prolonged pain, especially in advanced cases of cancer and also of neuritis from other cause. Toxicity of such preparations is not great, and the chief point to be kept in mind is that efficient dosage must be determined for each patient separately. The principal advantage of cobra venom therapy is that it is not depressing for the higher centers of the brain and that it can also be substituted gradually for the opium narcotics in cases of narcotic addiction.

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Macht, D. I., and Brooks, D. J.: Am. J. Physiol. **129**: 410, 1940.
Poole, W. B.: M. Rec. **153**: 287-291, 1941.
Rottmann, A.: Deutsche med. Wchnschr. **66**: 897-930, 1940.

LOW CHOLESTEROL DIETS

To the Editor:—What is the present opinion regarding low cholesterol diets in patients who have had coronary thrombosis? Please give references to the cholesterol value of foods.

M.D., Tennessee.

ANSWER.—The value of low cholesterol diets in coronary thrombosis is not clearly established. In some instances such a diet reduces an abnormally high serum cholesterol to a normal level; in others it has little or no effect. Factors other than the cholesterol content of the diet may be important in maintaining a high serum cholesterol level; namely, the level of metabolism, the state of hepatic function and the type of food which the body converts into cholesterol. Little is known about what "precursors" are important in human nutrition.

A complete table of cholesterol value of foods is given by Okey, R.: Cholesterol Content of Foods, *J. Am. Dietet. A.* **21**:341 (June) 1945.

PENICILLIN IN OIL IN PEDIATRICS

To the Editor:—Is the adult dose of 300,000 units of penicillin in oil harmful to an infant or young child?

L. Gruenewald, M.D., Sheboygan, Wis.

ANSWER.—The dosage of 300,000 units of penicillin in oil will not cause any damage to an infant or a young child.

DIPHTHERIA VIRULENCE

To the Editor:—In *The Journal* on page 955 of the issue of April 3, 1948, I note an affirmative answer to an inquiry concerning the virulence of diphtheria bacilli, "Can the same organism found to be nontoxic by guinea pig inoculation on one occasion be capable of changing its virulence after repeated cultures or after repeated animal or human passage?"

So far as I know there is no sound basis for this answer. All evidence is to the contrary, i. e., that diphtheria bacilli whether toxigenic or nontoxigenic remain unchanged in regard to these properties. Possibly the only suggestive results were obtained by Roux, who thought that he had altered the virulence of diphtheria bacilli, but his controls were not clear and no other conclusive experiment on these lines has ever confirmed him. One or two reports of alterations in virulence of toxigenic diphtheria bacilli include alteration in morphology and fermentative characters so that the organism of changed virulence is no longer recognizable as a diphtheria bacillus and may actually represent contamination.

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CONGENITAL CATARACTS

To the Editor:—I read with some interest your reply to "M.D." questioning the treatment of congenital cataracts (*The Journal*, volume 136, page 809).

Perhaps in the broader sense your reply is quite correct. It is, however, important that the child in question should develop fixation. The macula, as is well known, is not developed at birth, and subsequent growth appears dependent on the stimulus of surrounding objects. This, of course, is not likely when congenital cataracts exist—provided they are total. The prognosis when fixation nystagmus has developed is not good.

Nor would I be too optimistic about the late prognosis in the patients. They appear noticeably susceptible to major complications following intraocular surgery. Detachment of the retina and late secondary glaucoma are common causes for loss of vision in early adult life.

Dr. Arnold Knapp (*Arch. Ophth.* **32**: 405-406 [Nov.] 1944) discussed this matter thoroughly some years ago.

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